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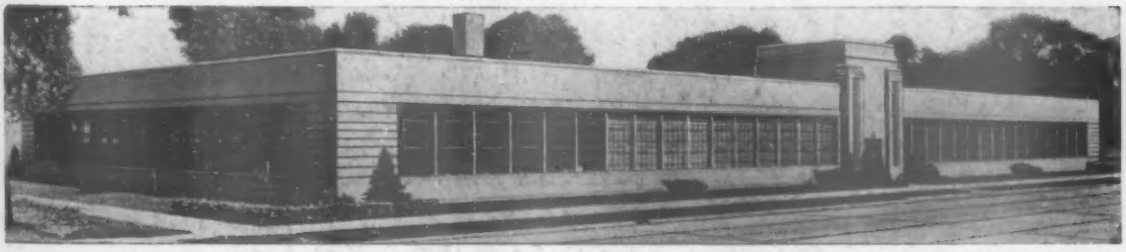

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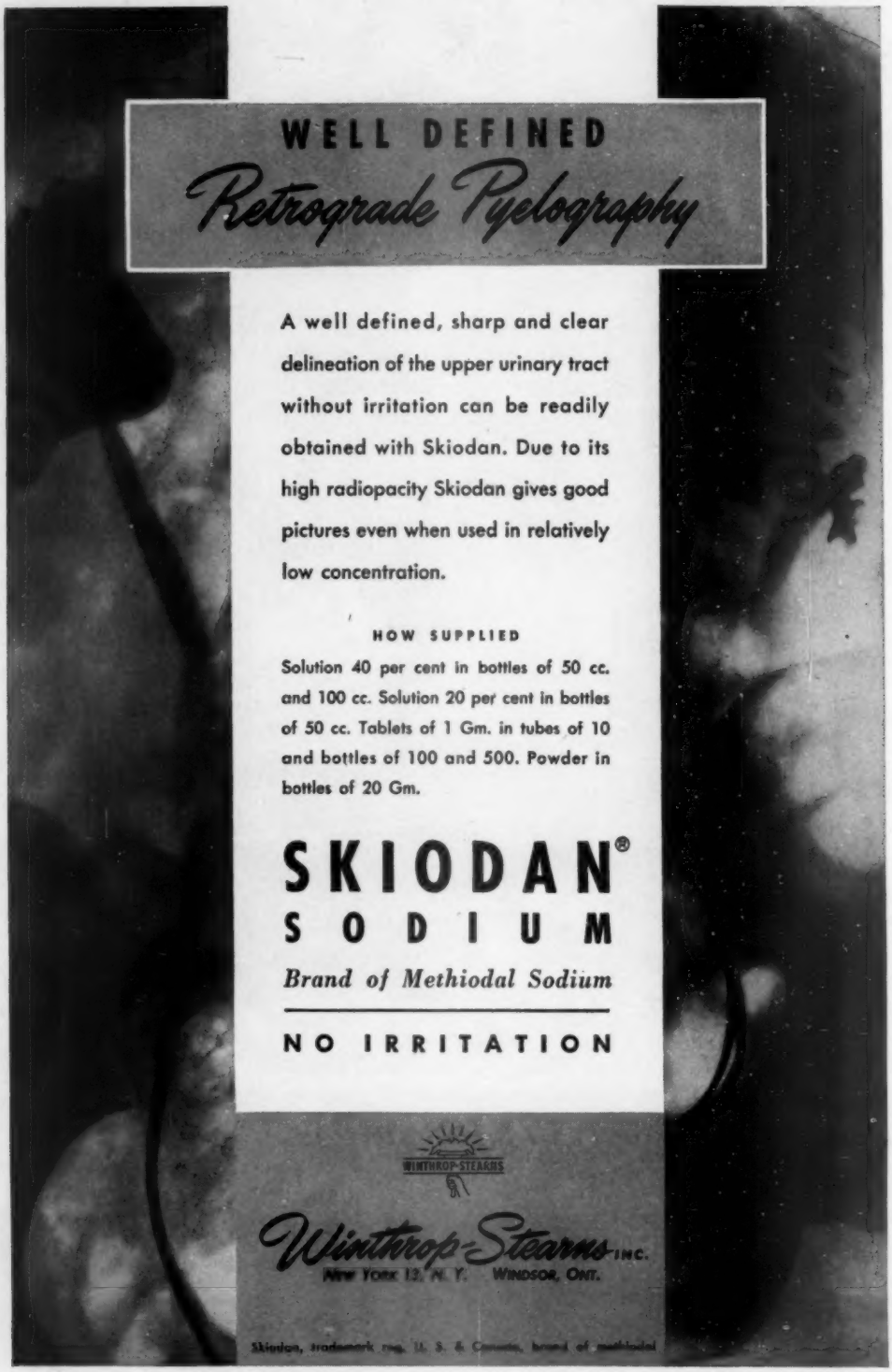
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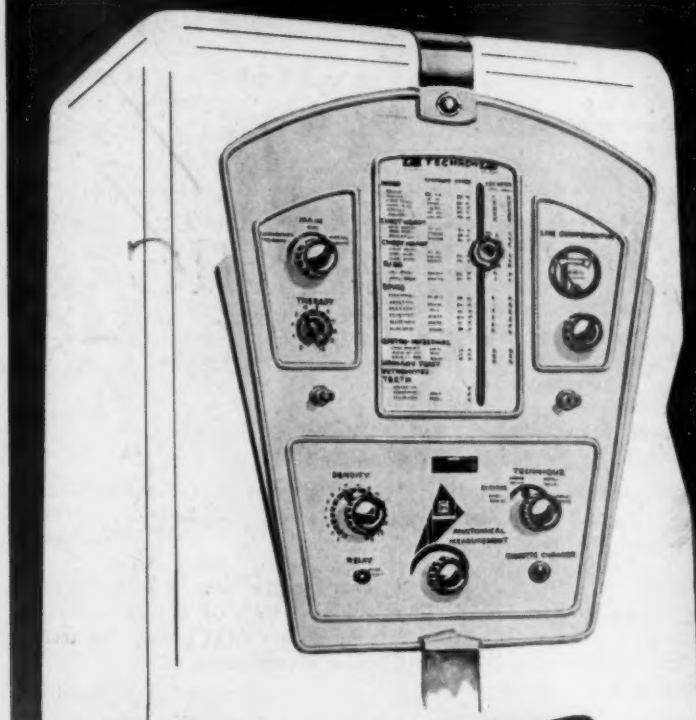

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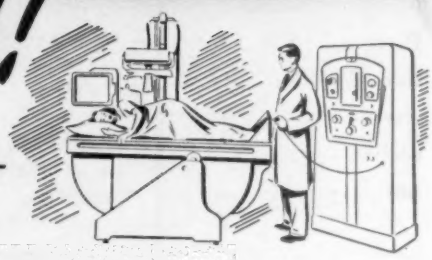

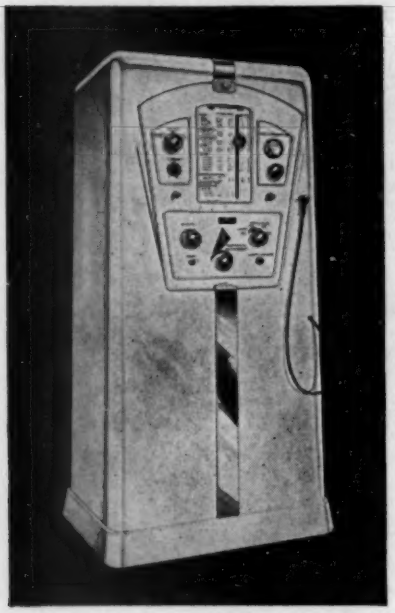

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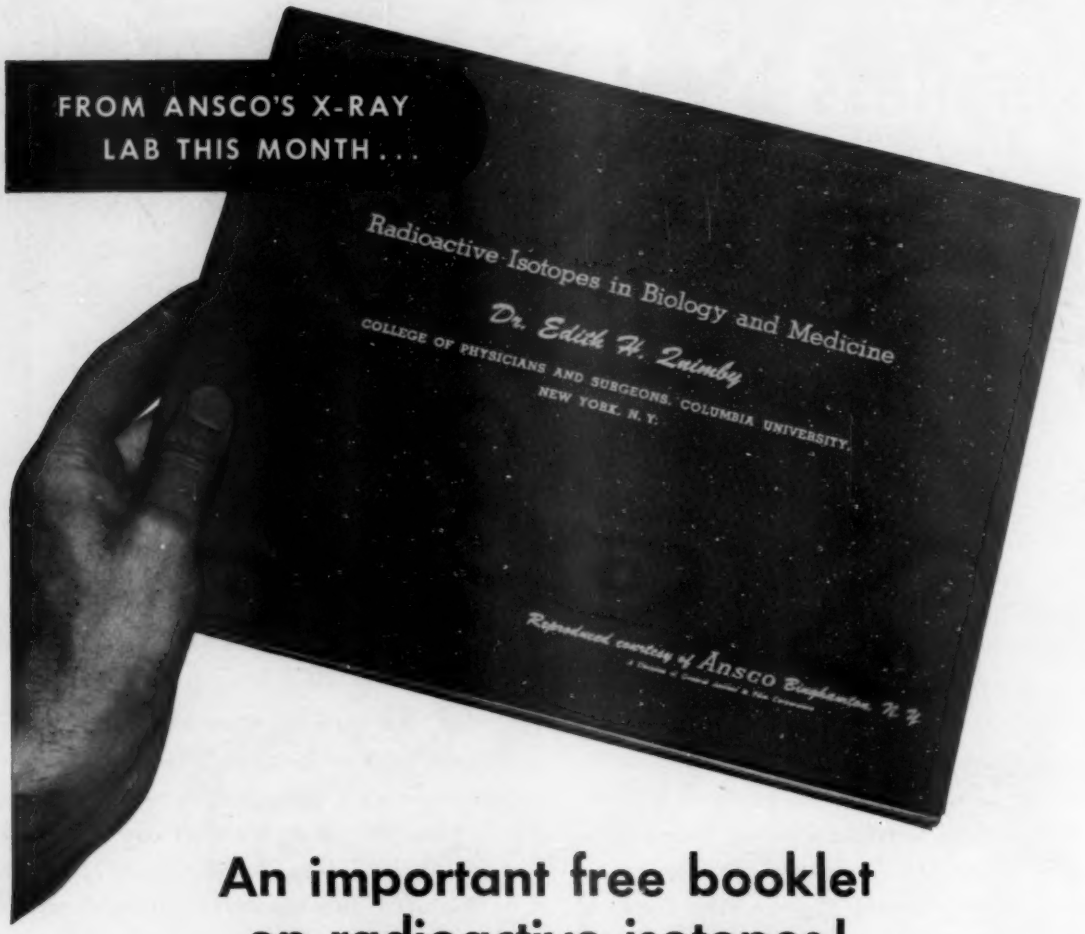
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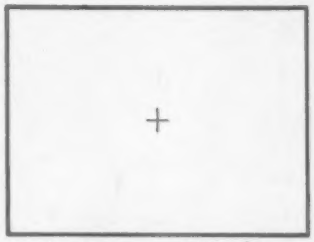

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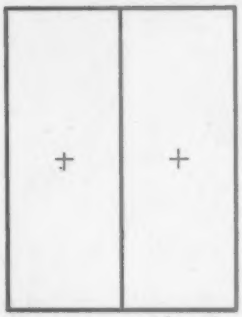

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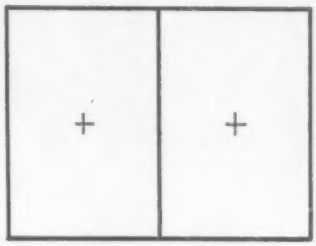

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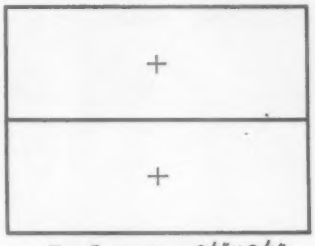

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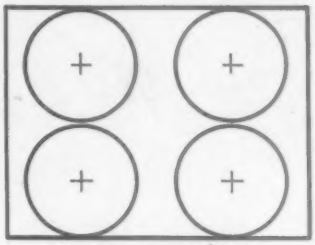

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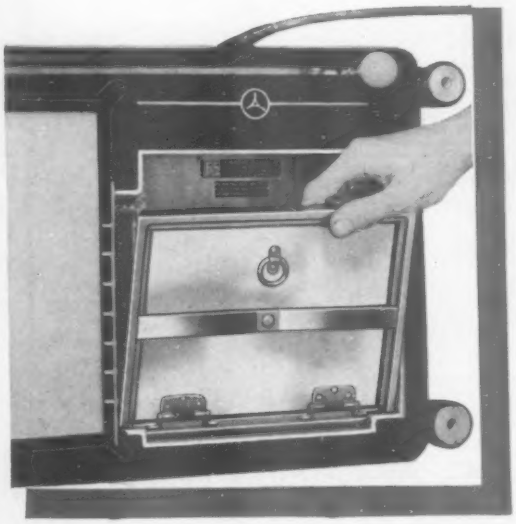

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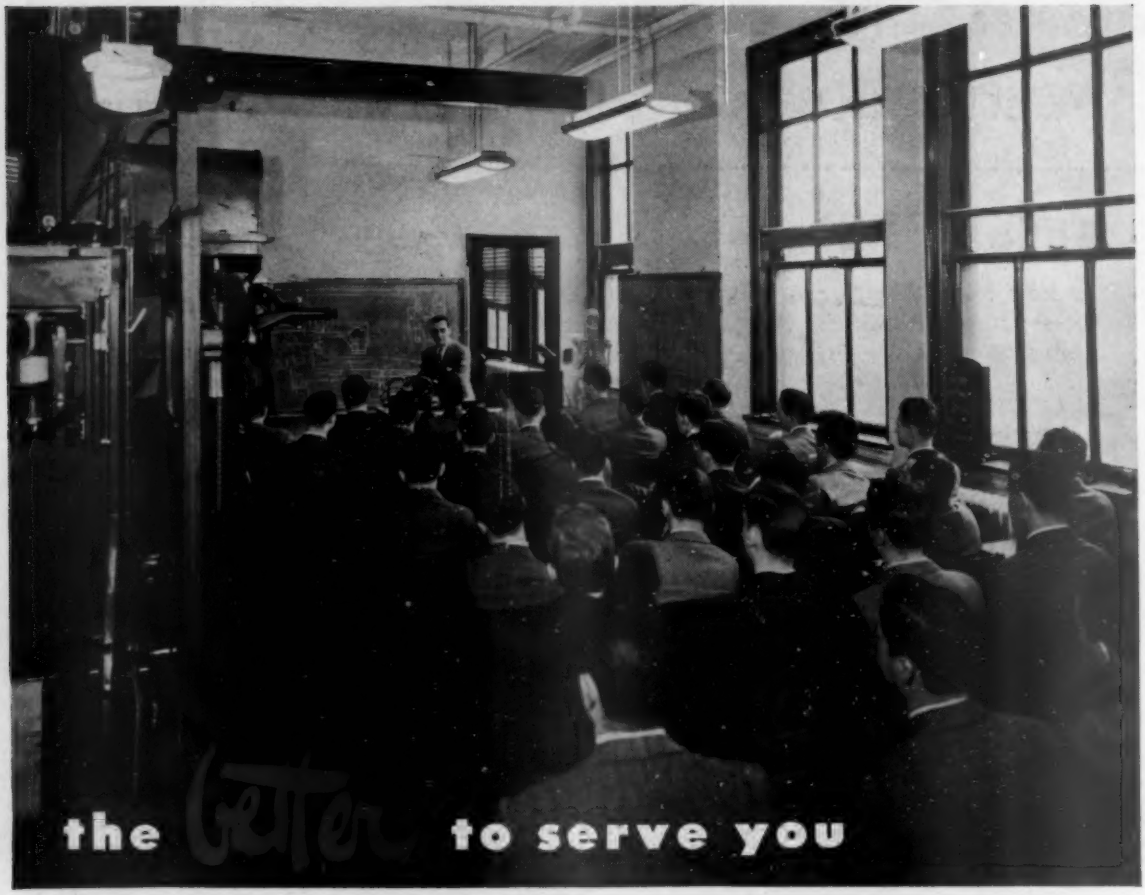

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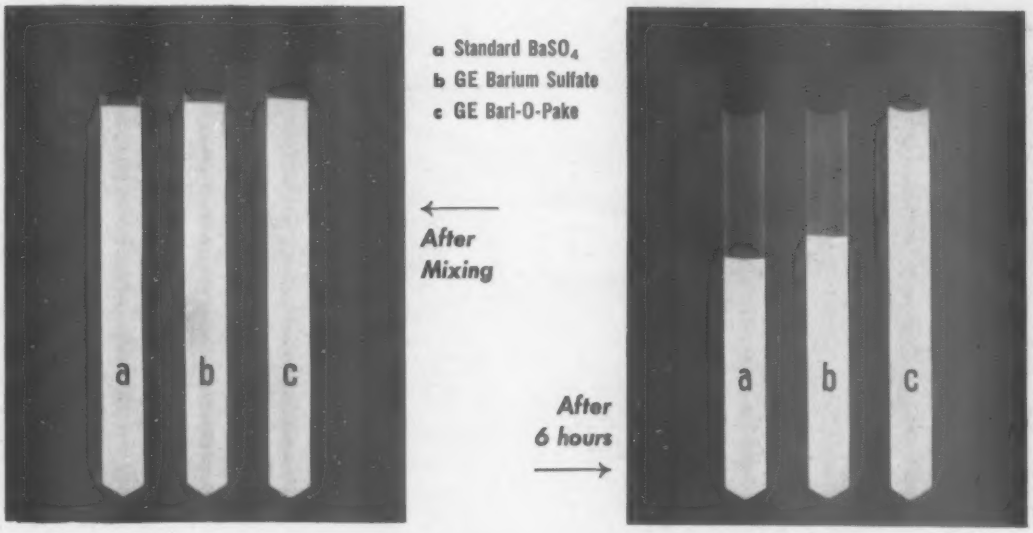

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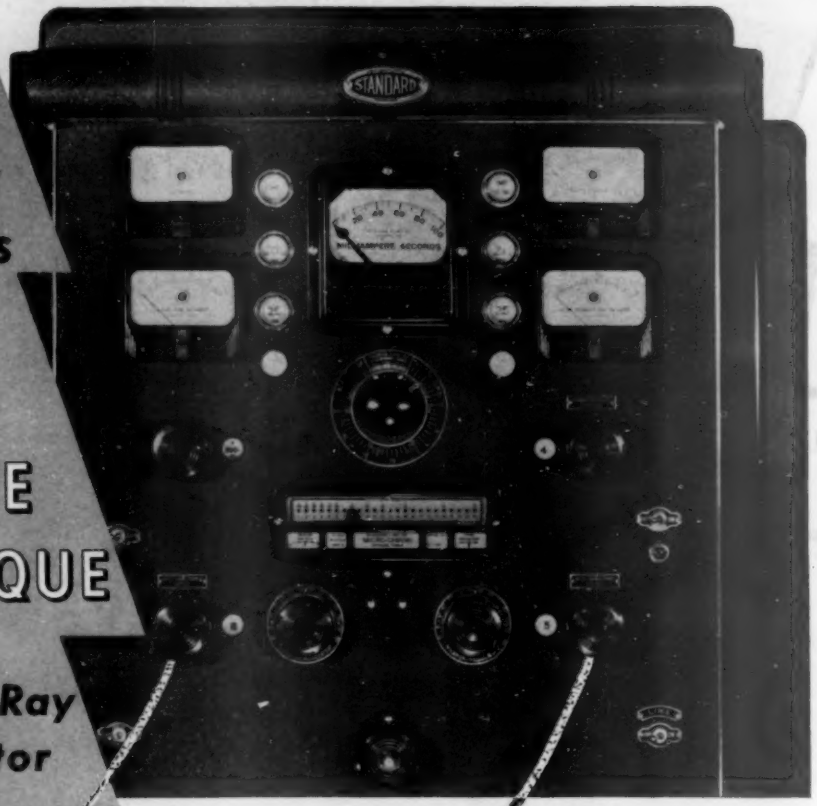

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ROSS GOLDEN, M.D., *Editor*

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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THE POSSIBILITIES AND LIMITATIONS OF ROENTGEN DIAGNOSIS*

PANCOAST LECTURE†

By LEO G. RIGLER, M.D.

MINNEAPOLIS, MINNESOTA

TO AN American physician, especially a radiologist, who has spent almost his entire life in the Middle West, a visit to Philadelphia is an emotional experience of large dimensions. For not only is this city the very birthplace of our country, but in almost similar fashion Philadelphia gave forth the wellsprings for the development of medicine in America. It is not surprising, therefore, that this community should have a most profound effect upon the development of the youngest of the medical specialties, radiology, during the half century which has passed since its inception. Some two years ago, on the occasion of the semi-centennial of the discovery of the roentgen rays, I undertook the task of reviewing the development of roentgen diagnosis in the United States[28] and I was struck, as any student of medical history would be, with the remarkable contributions of Philadelphia physicists and physicians to the establishment and the progress of radiology. One need only mention the names of Goodspeed, Charles Lester Leonard, Kassabian, Bowen, Snook, Newcomet, Willis Manges and, happily still with us, George Pfahler, to realize what this city has meant to this new science. In that development no one had a greater part than the man whose memory we come together to honor tonight. I am sure that all of you are familiar with the life of Henry K. Pancoast and with his accomplishments. I am sure that the distinguished physicians who preceded me in presenting this lecture have already, far better than could I, detailed some of the debt which radiologists, which physicians, which all people owe to Henry Pancoast for his unremitting devotion to the field of endeavor which he so richly endowed during the years which were permitted him. Perhaps I would do best to quote from the gifted pen of Percy Brown who wrote in this JOURNAL,[6] "For radiologists of the present and the future this life [the life of Henry Pancoast] is a pattern of a kind that all scientific men admire—clean-cut, smooth of edge, true of angle and of dimensional exactitude."

* From the Department of Radiology and Physical Therapy, University of Minnesota, Minneapolis, Minnesota.

† The Pancoast Memorial Lecture presented at the Annual Meeting of the Philadelphia Roentgen Ray Society, Philadelphia, Pa., November 6, 1947.

We who did not have the opportunity of working with him obtain from his writings the impression of a man of real intellectual honesty who faced every issue fearlessly and sought only for the truth. Scarcely any man in the history of American radiology has had more honors bestowed on him by his colleagues—certainly few have so well deserved them. A man who is privileged to present a lecture in honor of Henry Pancoast is fortunate indeed.

In a lecture memorializing the work of a great man it seems peculiarly fitting to discuss something which is related to the philosophy of the field in which he worked rather than to present any one specific investigation. Roentgen diagnosis having come of age, it is time to critically examine both the possibilities and limitations of a method which, because of its objectivity, because it appeals to the visual sense, in which we all have the greatest faith, has a certain attractiveness for physicians and for the lay public, inspires a certain confidence, not always completely justified by its accomplishments. The reliance which is placed upon roentgen study often goes far beyond the merits of the method. The contrary, of course, is also true, so that some definition of its limitations should be attempted. I use the term limitations in its broad sense, that is, as meaning the maximal as well as the minimal possibilities.

That there are situations in which disease processes are present without any roentgen evidences of abnormality whatsoever is well known. Likewise that positive roentgen findings may become apparent at a stage in the development of an abnormal process when symptoms, physical signs or any other evidences whatsoever are completely lacking is also known. Despite this there is relatively little written on this subject in textbooks or in current periodicals. It is difficult to find adequate discussion concerning the real significance of the negative roentgenogram in various diseases.[4,27] While the details of such structures as the lungs or the skeleton appear to be faithfully reproduced in the roentgenogram, a correlation of anatomical and roentgen findings reveals that many lesions which are microscopically apparent give no roentgen findings. It is evident that lesions must attain a sufficient size or produce sufficient changes before they have enough contrast density to be visible. Brailsford[3] has pointed to the most obvious example, pregnancy, in which the process must be present for at least nine or ten weeks before there is any chance of roentgen diagnosis. Another example which is known to all and fully described in most textbooks is acute osteomyelitis. Here the absence of roentgenologic signs for as long as two weeks—if an antibiotic or chemotherapy has been given the period may be even longer—after the onset of symptoms is a notable feature of the disease. Conversely, by means of roentgen examination of the stomach we have been able to demonstrate tumors as small as 5 millimeters and as large as 7 centimeters in diameter in patients who have no symptoms whatever.

There are three points of reference which one might use in determining the value of the roentgen method in the detection of an abnormal state at its earliest beginnings. The first would be the time of the actual onset of the disease, whether it be the day or hour of exposure, in the case of an infectious process, or the time of implantation of the tumor in the case of a neoplasm. In the former there is some possibility of determining this point of reference, particularly in such diseases as tuberculosis in which a specific exposure can often be clearly ascertained. In the case of neoplasms in humans it is impossible to state with any degree of certainty the exact time of inception. When such information is not available, as is the case in many lesions, another point of reference must be used, namely, the time of onset of symptoms. A third method of judgment rests in a quantitative determination of the size of the lesion necessary to be demonstrable by roentgen study.

To illustrate a method of procedure which should lead to a better understanding of the

limitations of roentgen diagnosis, I wish to present some data which we have collected concerning diseases of the thorax, data derived from experimentation, from case study, and from what might be called the past roentgen history. I hope to discuss briefly pulmonary edema, pleural effusion, pneumonia, chronic tuberculosis, acute miliary tuberculosis, metastasis to the lungs and, finally, bronchogenic carcinoma, from the point of view of the possibilities of roentgen diagnosis.

The rationale of this approach is based somewhat on the following experiences which, I believe, any roentgenologist is likely to encounter. A student discovers that the sputum of a patient whom he has examined contains a great number of tubercle bacilli. Characteristically, the student promptly appears in the Roentgen Department to have a roentgen examination of his chest and he wants to know at once whether or not he has tuberculosis. What answer should be given if his roentgenogram is negative? A patient comes into the hospital with high fever, leukocytosis and all of the symptoms of pneumonia. There are no physical signs. A roentgenogram is made, it appears to be negative, and the intern comes to ask, "Well, what does this mean? Does this patient have pneumonia even though the roentgenogram is negative?" A patient comes in with a very acute fever of perhaps a week's duration. He has cyanosis and tachypnea; the diagnosis of acute miliary tuberculosis is entertained because of his condition. Roentgen examination is made and the film appears to be entirely negative. What shall we say as to the diagnosis at this time or what criteria do we have for establishing the reliability of the roentgen study under such circumstances?

PULMONARY EDEMA

Many pulmonary lesions may well be classified into two categories: those which predominantly affect the alveoli and those which are essentially interstitial. The roentgen findings are usually obvious at an early stage in the alveolar type of lesion and are readily observed even when the findings are minimal. The converse is true of the interstitial processes which present recognizable changes in the roentgenogram only after complete development of the process. Pulmonary edema of ordinary clinical significance is usually a process in which there is exudation of fluid into the alveoli as a result of cardiac failure, overloading of the circulation, hypoproteinemia, renal failure, as well as many other conditions. There is, however, also an interstitial edema which seems to be associated with inflammatory processes and, curiously enough, seems to occur in animals as a result of circulatory failure. The difference in the time of appearance of roentgen findings noted above is true of these two types of edema as well as in the two types of inflammatory processes.

We have had occasion to study a large number of patients developing pulmonary edema either postoperatively[19] as a result of overloading of the circulation during a period in which the myocardial capacity is somewhat impaired or in the usual medical conditions. We have learned that this type of pulmonary edema can be demonstrated quite effectively on the roentgenogram at a time when the symptoms are minor or difficult to interpret and the physical findings are either minimal or completely absent.

To illustrate, the following 2 cases are reported because they demonstrate how rapidly changes may appear in a roentgenogram of the lung, and how sensitive the roentgenogram is as an indicator of the presence of fluid in the alveoli.

Case 1. A patient with glomerulonephritis had had a period of hypoproteinemia accompanied by generalized anasarca, extensive pulmonary edema and pleural effusion. She had recovered completely from this attack, the roentgenogram of the lungs was entirely clear; there were no physical findings whatsoever and the peripheral edema had disappeared completely. She was about to be discharged from the hospital when the intern came in to see

her and she complained that she did not feel quite as well as she had the day before. There was a slight increase in her respiratory rate but little else was obvious. She had been seen early that morning and appeared quite normal. The physical findings were entirely negative. Within two hours of the first onset of this slight dyspnea, a roentgenogram of the chest was made and showed definite edema in the lungs as manifested by the usual mottling and increased density along the vascular trunks. Within another six hours the changes were more prominent and the full blown picture of typical pulmonary edema appeared.

An even more striking illustration of the roentgen demonstration of edema is illustrated by the following case report.

CASE II. A patient with Addison's disease was being studied by Dr. Gerald Evans and his associates concerning the effects of the administration of desoxycorticosterone acetate and high salt intake upon the size of the heart. Roentgenograms of the chest were being made at frequent intervals with a view to determining the relative changes in cardiac size. During the course of these examinations this patients showed in addition to the tuberculosis of the adrenals, that there was an actual tuberculosis of the lung. The heart was very small, the lungs were dry and anemic looking, during the periods of addisonian crisis. There were several periods of treatment during which salt and desoxycorticosterone acetate were given and then withdrawn. On one of these occasions when a roentgenogram of the heart was made at a time when there were no symptoms nor physical signs whatever to suggest any abnormality in the lungs, clear evidences of pulmonary edema in the bases of the lungs were apparent (Fig. 1). The findings were so suggestive that the attention of the clinicians was directed to it at once. Even after looking at the roentgenogram and being given the opinion that pulmonary edema was present they re-examined her lungs, with negative results. There were, likewise, no evidences whatever of subcutaneous edema. A review of the careful studies of the blood volume, which were being made daily, indicated that on this day a striking dilution of the blood with retention of chlorides was present, so much so that pulmonary edema might readily have resulted.

FIG. 1. Case II. Pulmonary edema, early stage. The roentgen findings of streaked mottled, diffuse density at both bases were present before the appearance of obvious symptoms or physical signs. The presence of edema was confirmed by the laboratory findings.

Comment. Both of these cases demonstrate how sensitive the roentgen examination is as an indicator of the presence of pulmonary edema.

Another illustration to demonstrate the early evidences of pulmonary edema in the roentgenogram is afforded in patients who are having surgery on the thorax and who are not infrequently put in various positions in which the circulation to the lung is greatly hampered. Under such circumstances edema of one lobe or one lung may readily develop. We have made roentgen studies on the operating table of a number of such cases in which some suspicion appeared in the mind of the surgeon because of the behavior of the patient that edema or atelectasis might be taking place and we have been able to demonstrate the findings of edema in the dependent lobe within a few minutes after it occurred.

In experiments made on goats by Nessa and myself we attempted to demonstrate the earliest stage in which edema could be clearly delineated in the roentgenogram. The animals were put in the supine position which was throught would result in severe

circulatory failure. Pulmonary edema was thought to occur early. We were chagrined to find that roentgenograms did not reveal the kind of changes we have learned to expect in edema and only late in the course of the process did some findings appear. These were difficult to interpret and were certainly not at all characteristic of our findings in pulmonary edema. However, on microscopic examination of the lungs in these animals we found that they did not develop fluid in the alveoli, the kind of pulmonary edema we are accustomed to seeing in cardiac failure, but rather fluid and infiltration in the interstitial tissues. Under such circumstances it appears that the roentgen findings are much less characteristic, far more difficult to interpret, and appear at a much later stage in the process.

PLEURAL EFFUSION

The sensitivity of the roentgen method for the demonstration of fluid in the thoracic cavity is well shown in patients with pleural effusion. In the case of transudation the point of reference must be quantitative rather than one of time since it is impossible to determine in most instances either from symptoms or from other evidence as to exactly when the transudate began to accumulate. In the case of exudates there are usually symptoms which give a point of reference.

Experiments with monkeys, performed by one of my associates in connection with some other work on pleural effusions, in which various fluids were introduced into the pleural cavity in known amounts, were recalculated on the basis of the relative volume of the thorax of the animals under consideration and that of the average adult. As a result of this it appears probable that a minimum of 100 cc. of fluid in one hemithorax of the average adult is required for demonstration by roentgen study and then can only be seen if the lateral decubitus position is used. By using the lateral decubitus position, in clinical cases, we have been able to demonstrate very small quantities of fluid repeatedly, when physical findings were absent, as previously reported.[23,24] On the other hand, if reliance is placed upon the usual upright film made in deep inspiration, fluid may not be apparent in the roentgen study when there are already some physical findings. Under such circumstances the quantity of fluid must reach 300 to 400 cc. before there are roentgen changes. Another indication of the presence of small quantities of fluid lies in the appearance of the shadow of the interlobar fissure when the position of the patient is changed from upright to supine or prone. This is, of course, particularly true on the right side.[25]

PNEUMONIA

In the case of pneumonia it is rather difficult, of course, to establish the exact time when the infection occurred, at least in terms of hours. We can, however, in a few cases get a point of reference from the symptoms of the patient. This is, of course, particularly true of the bacterial pneumonias, the so-called lobar pneumonias, in which not uncommonly, the onset is sudden and sharp. We have made some efforts to obtain roentgenograms on patients very shortly after their first complaint. In many cases, because of a special combination of events, we have been fortunate in securing films on patients with pneumonia at a far earlier stage in the course of the disease than commonly happens.

It should be noted that the demonstration of consolidation in the lung is attended by many sources of error. Lateral views are often necessary[31] and particularly is it important to observe the density of the cardiac shadow.[26] The reports in the literature reflecting on the absence of roentgen findings when pneumonia is actually present are often the result of poor observations, especially the failure to take the above points into consideration. To illustrate the possibilities of early roentgen diagnosis in bacterial pneumonia, the following 2 cases will serve.

Case III. A male presented himself with the following clear-cut history. He said he was

perfectly well until a sudden onset of chills and fever and pain in the chest brought him to the hospital. The onset was very sharp and his history appeared to be very reliable. A roentgen examination (Fig. 2) was made one and a half hours after the first symptoms and already a triangular shadow of increased density, streaked in appearance and very characteristic of the very early stage of so-called lobar or bacterial pneumonia, is apparent in the right upper lobe.

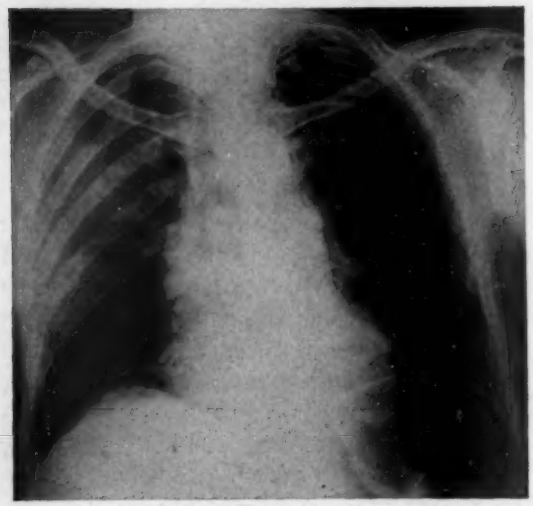

FIG. 2. Case III. Lobar pneumonia, one and a half hours after onset. The roughly triangular area of increased density in the right upper lobe exhibiting characteristic linear and homogeneous shadows is typical of lobar pneumonia in the early stages. Twenty-four hours later the entire lobe was densely consolidated.

Twenty-four hours later the process became extremely dense, went on to involve the entire lobe in perfectly characteristic fashion and the more typical appearance of lobar pneumonia was found. This was a pneumococcus type pneumonia.

CASE IV. A child was coming to our outpatient clinic for another condition. He was seen late in the afternoon, his temperature was taken and various other examinations were done and at that time he was apparently perfectly normal. He had to remain over for further examination the next day so he went to a motion picture theater that evening where he suddenly was taken with severe pain in the side, began to cough, and felt very uncomfortable. This persisted so that he had to leave the theater and finally reported to our admissions department. A roentgen examination was made at once, just two and a half hours after the very first symptom. Here again, in the lateral view, the triangle of streaked density which is so typical of early lobar pneumonia was found.

Thus we see that in 2 cases of bacterial pneumonia an hour and a half and two and a half hours after the first onset of symptoms, diagnostic roentgenograms were apparent. In our experience in such cases some physical signs also appear very soon after the appearance of roentgen signs. We have studied some 20 fairly well controlled cases of similar character and it is our impression that practically all cases of bacterial pneumonia of the ordinary type will give positive roentgen signs within twelve hours and in the majority of cases within six hours after the first onset of symptoms.

In the case of the atypical or virus pneumonias the situation is completely different and it is interesting to note that these are really interstitial processes at the beginning whereas the bacterial pneumonias start with an intra-alveolar exudation. The difference in the pathologic findings likewise produces a sharp change in the time of development of roentgen findings. In atypical pneumonia twenty-four and even forty-eight hours may elapse before one can make a definite determination of an abnormal process in the roentgenogram, although the patient's symptoms are outstanding. The physical findings are even slower in their appearance and the roentgen findings almost always precede the physical signs. There are, of course, cases in which the roentgen findings are readily apparent although the patient has very few symptoms. But when the time of onset is known, it will be usually found that a fairly long period has elapsed before the roentgen findings appear.

CASE V. A white male, aged twenty-four, was admitted to the hospital one week after the onset of symptoms. The illness began with a chill and there had been daily temperature elevations as high as 102° F. Persistent cough with expectoration of mucopurulent sputum was present. There were a few crackling rales

over the right lower lobe. The white blood count was 11,000 with 81 per cent neutrophiles. The sputum showed only micrococci and staphyloccoci. Later studies of the sputum, the reaction to therapy and the temperature curve all suggested a fairly characteristic picture of atypical pneumonia. On roentgen examination, however, only a few faint changes were made out in the lower lobes which were rather difficult to interpret. They may well represent interstitial infiltrations, but are not at all characteristic.

Comment. This is an example of an atypical pneumonia present for almost a week yet giving roentgen findings which might well be considered essentially negative.

A negative roentgenogram, therefore, twelve hours after the onset of symptoms suggesting lobar pneumonia is of great significance. In patients with symptoms of atypical pneumonia, however, forty-eight hours must elapse before negative findings can be considered at all conclusive.

CHRONIC TUBERCULOSIS

Many years ago McPhedran[14] and Opie[20,21] directed attention to the latent period which usually elapses between the appearance of the roentgen signs of pulmonary tuberculosis and the development of symptoms. In 1934, we[29] used the term "latent period" to designate the delay between the exposure to the tuberculous infection and the development of roentgen findings. We reported a series of 5 cases of pulmonary tuberculosis in young adults whom we had the opportunity to observe frequently and whose history of exposure and tuberculin skin test was known. Recently there have appeared an editorial[4] and papers[3,5] by Brailsford in which he likewise directs attention to this latent period between the beginning of a disease and the development of roentgen signs. Brailsford also emphasizes tuberculosis since it is of considerable importance to know the significance of negative roentgen findings in relationship to the time exposure due to tuberculosis. That some delay must occur is evident. Such an interval may account, in part at least, for the failure to sift out all cases of tuberculosis in induction centers, for example, or in tuberculosis surveys.

We have now collected 13 cases in which we have been able to ascertain data similar to those previously reported. In these patients negative skin tuberculin tests and negative roentgenograms are on record on repeated occasions. The time of exposure to a known case of tuberculosis is fairly clear. From three to five weeks after the exposure there is a conversion of the tuberculin test from negative to positive. In some cases we have roentgenograms made four, five and six weeks after the tuberculous exposure with negative results. Then at ten to twenty weeks positive roentgen findings appear and further study for a number of years confirms the diagnosis of tuberculosis.

It should be noted that these cases are of a particular character since they are young adults apparently tuberculosis free before exposure, yet the roentgen findings suggest what is usually designated as reinfection tuberculosis. I should emphasize that none of these patients had symptoms at the time of the discovery of the lesion although they developed symptoms later. An illustrative case of this type is described below.

Case VI. A nurse, aged nineteen, had been examined several times. Her tuberculin skin test was negative and the roentgenograms of the chest were negative. She was exposed to tuberculosis in a group of patients. Five weeks later her tuberculin skin test was found to be positive. At the same time the roentgen examination was negative (Fig. 3*A*). Ten weeks after exposure a small area of infiltration measuring about 10 mm. in diameter appeared in the left subclavicular area (Fig. 3*B*). There was some evidence of exudation about it. There were no clinical symptoms nor physical signs. Five months later the lesion showed some diminution in size and appeared denser and more fibrotic. The shadow remained about the same thereafter.

It is interesting to note that Malmros and Hedvall,[11] in a monograph on the development of tuberculosis published in 1938, were able to collect a series of somewhat similar cases and in their group they

undoubtedly have been able to demonstrate, in a few cases at least, roentgen findings eight weeks after the first exposure to tuberculosis. The latent period, here described, is no doubt dependent upon the size of the lesion and it is significant that there is a close correlation with the experimental work on tuberculosis in animals. It takes about six weeks after the usual type of induction of experimental chronic tuberculosis in animals for tubercles to coalesce in characteristic fashion. Obviously some further time has to elapse before these microscopic tubercles enlarge sufficiently to arrive at a size of nodule which is demonstrable on the roentgenogram.

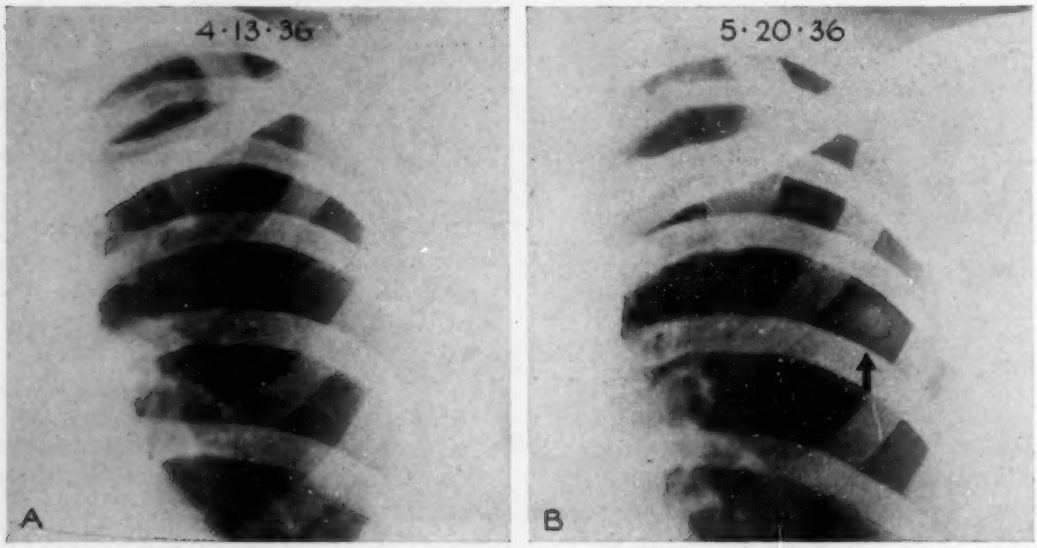

FIG. 3. Case VI. Pulmonary tuberculosis with early roentgen findings. *A*, roentgenogram, left upper lobe, made five weeks after exposure to tuberculosis, immediately after conversion of tuberculin skin test to positive. The area appears entirely normal. *B*, roentgenogram of same area five weeks later and ten weeks after exposure to tuberculosis. Typical findings (arrow) indicative of tuberculosis are shown. The shadow was reduced in size and gave a more fibrotic and nodular appearance in roentgenograms made five months later.

Dale[7] has reviewed the whole subject of the visibility of small lesions in the lung in great detail, particularly with reference to early tuberculosis and miliary tuberculosis. McPhedran,[12,13] and a great many others, have done many experiments in an effort to demonstrate what size a single lesion must attain to be visible in the roentgenogram of the adult chest. McPhedran[13] showed that lesions of 1.5 to 2.0 millimeters in diameter could be demonstrated in the inflated lung removed from the thorax. McPhedran and Weyl[15] have indicated some of the technical factors involved in the demonstration of small tuberculous lesions. Morgan[16,17,18] has recently reviewed the technical factors in the demonstration of small shadows. Experiments which Dr. Joseph Jorgens has been conducting on living individuals under favorable technical conditions and also with the use of a phantom have up to this time indicated our inability to satisfactorily demonstrate a single lesion in the living individual less than 3 millimeters in diameter. In the phantom 2 millimeters appears to be the minimum. Further experiments are being carried in on this direction.

ACUTE MILIARY TUBERCULOSIS

In connection with this, the matter of acute miliary tuberculosis is of great importance. I believe every experienced roent-

genologist and phthisiologist would agree, with only very minor exceptions, that individuals who have symptoms which are the result of chronic parenchymal pulmonary tuberculosis will exhibit demonstrable roentgen signs. Patients with symptoms usually have sufficient exudation so that the roentgen examination is positive. There are some exceptions, of course, to this rule. In most cases, the exceptions, I believe, will be found to be, not the usual parenchymal tuberculosis, but rather bronchial tuberculosis in the early stages before there is appreciable parenchymal extension or bronchostenosis. In such situations, i.e., a pure bronchial tuberculosis, symptoms such as hemoptysis may be present, the sputum may contain tubercle bacilli without definite roentgen findings being exhibited. This might well be expected from the anatomy of the process.

In the acute pulmonary tuberculous processes, particularly acute miliary tuberculosis, the dictum that roentgen findings precede symptoms does not hold. In a large percentage of the cases of acute miliary tuberculosis the roentgen findings are completely absent at the first onset of symptoms and often for a long period of time thereafter.[1,7,9,8]. So far as we can determine from correlated studies of autopsies and roentgen examinations the difference lies largely in the number and size of the tubercles which are present.[22] When one considers that the usual miliary tubercle is less than 1 millimeter in diameter it becomes evident at once that some other factor must be present in order to give the striking picture which acute miliary tuberculosis frequently exhibits. This additional factor has been the subject of a good deal of discussion but it seems to me it has been fairly well established that it is largely a matter of superimposition. If a sufficient number of these small 0.5 or 1 millimeter sized tubercles are lined up, a sufficient density will be produced to give the shadow which is seen in the roentgenogram and until that time the roentgenogram may appear to be completely negative.

In some cases striking and characteristic findings will appear within a week or ten days after the onset of symptoms. In many, however, as long as six or eight weeks may elapse. The following case demonstrates the latter finding.

Case vii. A patient who had a mass in the mediastinum, which was thought to be a dermoid cyst, was admitted to the hospital and was operated upon. The cyst was found but owing to inflammatory adhesions could not be entirely removed, so was drained. Shortly thereafter she developed a fever which rapidly became severe, dyspnea developed and seven weeks later she died. Roentgen examination of the chest was made on several occasions, the last being six days before death, and the appearance was normal except for the tube draining the mediastinum. At autopsy, numerous miliary tubercles measuring from 0.5 to 1 mm. and a few 2 mm. in size were found. These were largely on the pleura and were rather widely, but thinly, distributed. There were some in the lungs as well. The number was much less than is usually the case and I am inclined to believe that this is the explanation for the failure to observe any changes on the roentgenogram.

Comment. Six weeks after the first ontse of symptoms of miliary tuberculosis, a satisfactory roentgenogram of the chest failed to reveal any evidence of the disease. We have seen many other cases of the same type. A negative roentgenogram, therefore, even six weeks after the onset of severe symptoms, does not exclude acute miliary tuberculosis. Roentgen findings may be present but frequently are not.

METASTASIS TO THE LUNGS

That very small lesions in the lungs can be demonstrated effectively by roentgenography is best shown in the case of metastatic processes particularly such as occur from sarcoma, from Ewing's tumor and also, in all probability, from carcinoma. We have been able to observe a number of such cases and to have the opportunity to demonstrate the difficulties and the advantages of roentgen examination in this situation. Here we have a condition in which the roentgen findings invariably pre-

cede the symptoms and the physical signs; they certainly appear at a very early stage in the development of the lesion. It is, of course, impossible to say when the lesion actually began. Brailsford[5] has said that he could demonstrate metastases from sarcoma within two weeks of their dissemination but he has made the assumption that the dissemination occurred on the day of amputation, an assumption which is scarcely valid. We have studied a number of such cases intensively and I should like to report one of these to illustrate our observations.

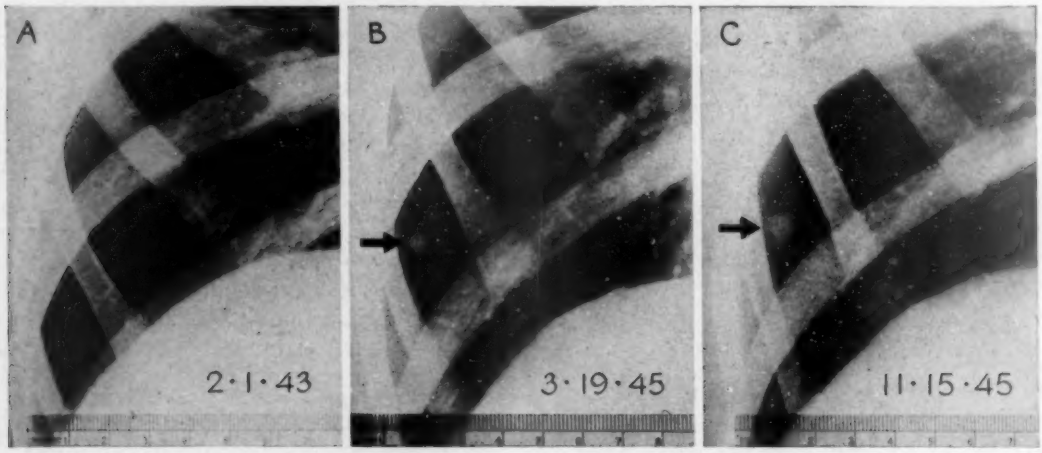

FIG. 4. Case VIII. Metastasis to lung from Ewing's tumor. *A*, roentgenogram, segment of right lower lobe, made at time of amputation. Normal. *B*, same segment about two years later. Note small nodule measuring 3 mm. in diameter clearly visible. This approaches the minimum size permitting roentgenographic detection. *C*, same segment eight months later. Note increase in size of metastatic nodule which now measures 7 mm. in diameter.

CASE VIII. A male, aged fifteen, developed a Ewing's sarcoma of the tibia; amputation was done and it was followed by irradiation. His lungs were being examined at semi-annual intervals with a view to finding metastasis. The roentgenograms (Fig. 4*A*) appeared entirely normal until about two years after amputation when the first change was observed; that is, an extremely small nodule measuring about 3 mm. in diameter in the roentgenogram was seen (Fig. 4*B*). It was clearly visible because of its location well out at the periphery of the lung where the contrast with the surroundings was striking. This being the only lesion in the lungs we were in some doubt, naturally, as to the exact diagnosis, although it was felt that a metastasis was probably present. Eight months were allowed to intervene before a re-examination was done and at the end of that time the lesion appeared to have grown in size so that now it measured about 7 mm. in diameter (Fig. 4*C*). At this time since no other lesion could be found, a segmental pneumonectomy was performed by Dr. John Paine and Dr. Richard Varco. The specimen showed a typical metastatic nodule actually measuring about 6 mm. The patient recovered promptly and without incident. He was re-examined again about seven months later. The lesion on the right was entirely absent and there were no residual evidences of the surgery, but now a similar nodule became apparent on the opposite side. It was not clearly recognized at this time, but on re-examination six months later it was observed. At this time a segmental pneumonectomy was performed on the left and a similar tumor removed. There was already another metastasis on the right but it was so small that it was not observed. Six months later several metastases became clearly evident. The differentiation of such small lesions from vascular shadows is difficult but may be accomplished by making films in different phases of respiration, by rotation, or by timing the exposures in the cardiac cycle as described by McPhedran and Weyl.[15]

Comment. It is evident that in the case of metastasis exceedingly small lesions may be seen before there are any symptoms or physical signs.

There is, however, even here, another side of the question not commonly pointed out and that is the case of miliary metastases in which the lesions are less than 1 millimeter in size. If one follows patients to autopsy consistently, it is astonishing occasionally to find a patient whose pleural surfaces appear to be studded with tiny metastases yet the roentgenograms appeared to be entirely negative. A characteristic example is reported below.

Case IX. A patient with carcinoma of the esophagus was operated upon by Dr. Richard Varco. During the course of the exploration of the mediastinum he also explored the left lung and found numerous, exceedingly small miliary nodules over its surface. These were confirmed first by biopsy and later at autopsy as metastases from carcinoma. Yet a roentgen examination had been made the day before operation and nothing was seen but a few tiny shadows; they were indistinguishable from the vascular trunks. Even knowing the findings it is impossible by magnification or otherwise to demonstrate any abnormal shadows.

Comment. It is clear that metastases of 3 millimeters or over may often, although not always, be shown on the roentgenogram. Miliary metastases, like miliary tubercles, may readily escape detection.

BRONCHOGENIC CARCINOMA

Finally, with this same point of view in mind, I should like to explore one more field of roentgen diagnostic endeavor; that is, primary carcinoma of the lung. Here again we have no means for determining the time of onset but we do have evidence with regard to the first symptoms of the patient. The problem of whether or not we can determine the presence of a primary tumor in the lung by means of roentgen examination prior to the onset of symptoms is of considerable importance. The widespread trend toward mass surveys of the chest may well lead us in the direction of an attempt to diagnose such tumors in symptomless individuals more frequently than heretofore.

Because roentgenograms of the chest are made so commonly we have been successful in finding earlier films made in various institutions other than our own on a considerable number of patients in whom we have suspected or have demonstrated the presence of a bronchogenic tumor. We have thus obtained a sort of past roentgenologic history that has permitted us to get some idea as to whether or not carcinoma of the bronchus may be present with symptoms and without apparent roentgen findings or, conversely, whether the roentgen findings may appear in many cases before the onset of any symptoms whatever. Our experience in a number of cases indicates: (1) that with adequate examination the roentgen findings may well be evident in many cases at a time when the patient is apparently well; (2) that the roentgenologic findings are almost always present if the patient has symptoms; (3) that the cases in which physical signs and symptoms are present while there appears to be an absence of roentgen findings, adequate examination, particularly in different phases of respiration, will almost invariably produce roentgen evidences of abnormality.

In order that abnormal changes be observed in the early stages which we are considering, it is necessary to pay close attention to relatively minor changes in the normal lung pattern. Particularly is it necessary to determine differences in the degree of inflation of the lungs during the phases of respiration. I do not wish to go into the details of the roentgenologic findings in primary tumors of the lung. I would only point out three important signs which are exhibited in this series of roentgenograms, to which perhaps more attention should be given. Let me emphasize that none of the things that I shall speak of are necessarily pathognomonic of bronchogenic carcinoma. They represent, however, clues which should lead us to further

investigation and thereby the establishment of the diagnosis in more unequivocal fashion.

The first sign is enlargement of one of the root shadows of the lung. We all appreciate the great variation which exists in the size of the root shadows and the numerous lesions which may produce enlargement of one or both of the root shadows, leaving it as a residual but without present clinical significance. Nevertheless, in view of the increasing frequency with which carcinoma of the lung is seen and the extreme importance of the problem from the standpoint of the saving of many individuals it is incumbent upon us to give more attention to such minor changes.

CASE X. A patient came with pain in the fibula which proved to be due to a destructive tumor. On biopsy examination this was shown to be a metastatic adenocarcinoma. Routine examination of the chest (Fig. 5*A*) was then made and an enlarged root shadow on the right side was found. On the lateral view (Fig. 5*B*) this was clearly in the center of the lung around the bronchi. Further studies with bronchography and planigraphy revealed constriction of the right lower lobe bronchus characteristic of carcinoma. The lesion might well have been completely overlooked had it not been for the metastatic process which was already present. The patient had no pulmonary symptoms. (Previously reported.[19])

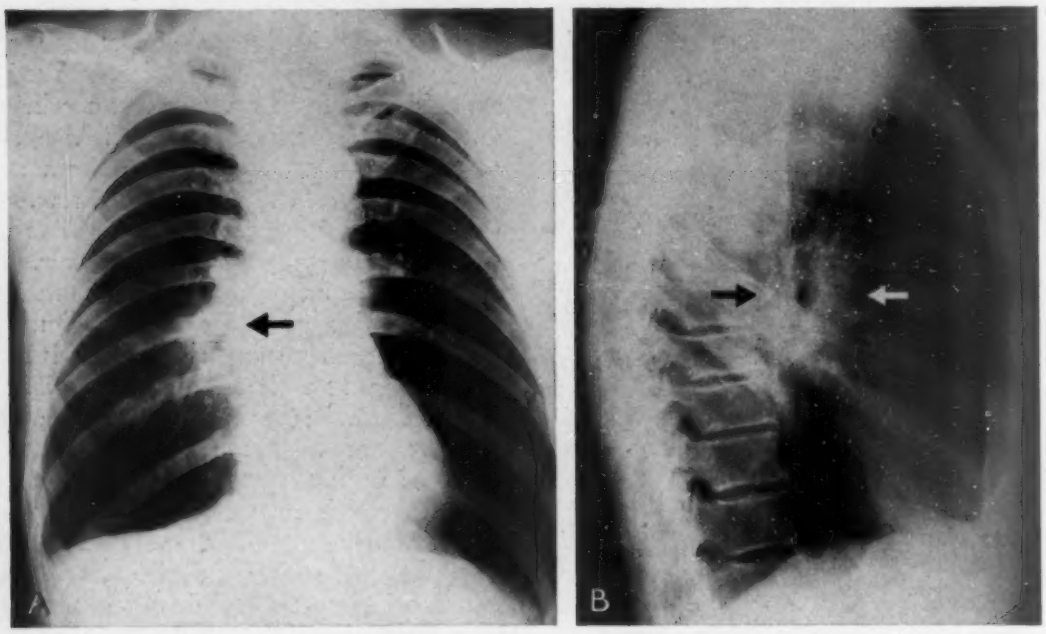

FIG. 5. Case x. Primary carcinoma, right lower lobe bronchus, without pulmonary symptoms found on routine examination. *A*, posteroanterior roentgenogram. Note enlargement of right hilar shadow (arrow). *B*, right lateral view. The enlargement of the root of the right lung with irregular radiating borders is well shown (arrows). There is a generalized emphysema of independent origin.

Comment. Unilateral enlargement of the hilar shadow in a symptomless individual might well be observed during the course of a mass survey and such cases should certainly be singled out for intensive study.

The second sign is an area of density in the periphery of the lung which may be round and sharply defined or irregular and poorly defined. In themselves such isolated shadows are difficult to distinguish from a variety of other processes such as tuberculoma, atypical pneumonia, benign tumors, localized abscesses or fluid-filled cysts. Nevertheless such a shadow may be the

first clue to the presence of a peripheral or infiltrating carcinoma of the lung and is often found accidentally. The significance of the peripheral nodule as an early sign of carcinoma of the lung in symptomless individuals has already been thoroughly explored.[2,10] I would call attention to other types of peripheral infiltration which are not so obvious. The following 2 cases illustrate minimal findings in the periphery of the lung, representing the first stages of carcinoma; they may be detectable in the roentgenogram before the onset of symptoms or may readily be overlooked even after the development of symptoms.

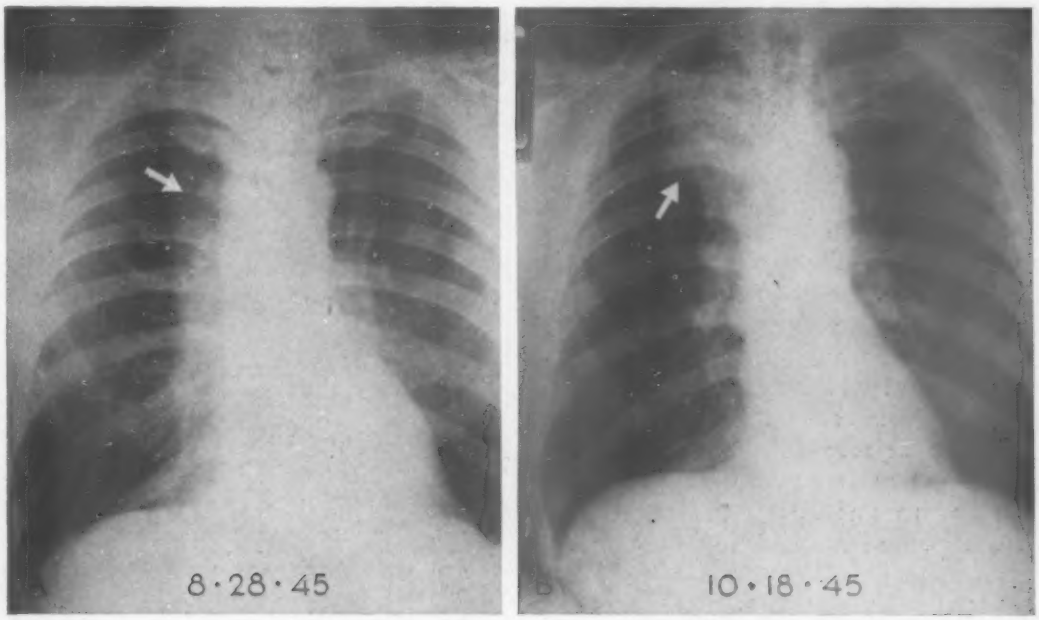

Fig. 6. Case xi. Bronchogenic carcinoma right upper lobe with symptoms and minimal roentgen findings. *A*, roentgenogram of right upper lobe, August 28, 1945, originally interpreted as negative. Note the very small nodule (arrow), the only evidence of the tumor at this time. *B*, re-examination of same area five weeks later. The lesion has grown in size and shows a fairly characteristic infiltration (arrow). (Courtesy of Dr. M. B. Hanson and Dr. Leo Nash.)

Case xi. A male, aged fifty-nine, consulted a physician in July, 1945, when he began to complain of respiratory symptoms. There was a cough productive of a whitish to yellow sputum and a low grade pain in the chest, localized over the sternum, accompanied by weakness, fatigability and listlessness. Roentgenograms of the chest were made elsewhere on August 28, 1945, and were considered to be negative (Fig. 6*A*). On re-examination, however, there is shown a very small density in the right superior mediastinum with slight enlargement of the hilar shadow. Because of the negative diagnosis nothing was done; the pain continued and became somewhat more severe. He was admitted to another hospital on September 29, 1945, where he developed chills and fever and a diagnosis of atypical pneumonia was made. Roentgenograms made on October 1, 1945 (Fig. 6*B*), show a definite infiltration of considerable degree in the right upper lobe extending out from the mass which was originally present in the films of August 28.

He was first seen here October 21, 1945, at which time he was seriously ill and a mass had developed overlying the sternum between the third and fourth interspaces on the right side. There were no physical findings so far as the lungs themselves were concerned, except for some dullness over the area of the mass. Bronchography was undertaken and no obstruction to the major bronchi could be made out. It was impossible to fill out the anterior branches of

the right upper lobe bronchus, however. Further examination showed destruction of the sternum and a mass extending to the left side.

The patient died on November 7, 1945. In the right upper lobe numerous nodules varying in size from 1 to 5 by 4 mm. in diameter were found. In addition there was a large lobulated lymph node measuring 8 by 5 cm. to the right and superior to the bifurcation of the trachea. In the microscopic section these appeared to be typical of small cell carcinoma characteristic of a primary lung tumor. Metastatic lesions were also found in the sternum, spleen, kidney and brain.

Comment. Here we see a lesion, present in the roentgenograms made after the onset of symptoms, but unrecognized because of its extremely small size. When it became large enough to give a more definite shadow metastases had already occurred. It is evident that primary carcinoma of the lung may, in some cases, give respiratory symptoms even when the tumor is of small size and difficult to detect in the roentgenogram; yet the demonstration of the nodule in the original roentgenograms bears out the dictum that roentgen findings will be visible if symptoms are present.

CASE XII. A white male, aged sixty-two, was first seen in this hospital in October, 1938.He came in complaining of headaches, and a maxillary sinusitis was found to account for this symptom. A routine film of the chest was made at that time and was reported to be negative. However, on re-examination, minor changes suggesting fibrosis and infiltration can definitely be made out in the right apex. There were no pulmonary symptoms at that time although the changes in the roentgenogram are quite definite. Three months later he began to have some pain in the chest, slight cough with some fever. In February, 1939, clubbing of the fingers was observed by his own physician. Two weeks later another roentgenogram of the chest was made and a definite mass could be made out in the right apex corresponding to the areas of infiltration shown in the film made five months earlier. Later the process increased in size and the patient finally died as a result of the lesion, having developed metastases to the liver.

CASE XIII. A male, aged fifty-seven, came in because of pain in the chest and cough. On the first roentgenogram there was observed an area of emphysema in the right upper lobe. In the inferior portion of the right upper lobe there could be seen a somewhat linear zone of density fairly characteristic of atelectasis. The whole right upper lobe was larger than normal and on expiration failed to contract as did the remaining portions of the right lung and the left lung. Thus the combination of atelectasis and emphysema from obstruction of the right upper lobe bronchus was clearly observed in this case at this time. The posteroanterior roentgenogram made in expiration is illustrated in Figure 7*A*. Planigraphic and bronchographic examinations revealed a characteristic carcinomatous obstruction of the right upper lobe bronchus which was later proved by bronchoscopic biopsy. The bronchogram is shown in Figure 7*B*. At exploration the extent of the lesion was such as to make extirpation impossible.

Comment. The combination of atelectasis and emphysema produced simultaneously by a tumor of the bronchus is illustrated in Case XIII. In most patients the emphysema appears first; the atelectasis is a late development. In this case the symptoms were already present at the time the roentgen findings were observed.

CASE XIV. An iron miner was examined elsewhere on repeated occasions to detect early silicosis. He had some complaint of pain in the chest in 1944, and some cough prior to that time but this disappeared. He was seen January 29, 1945, at which time he had no complaints whatever. Routine examination of the chest was made because of the possibility of silicosis. In the roentgenogram made at this time elsewhere, a local area of emphysema in the right upper lobe can be made out characteristic of the segmental obstructive emphysema described by Westermark as the first sign of obstruction of the bronchus (Fig. 8*A*). It should be emphasized that there were no symptoms at this time. Several months later he began to have a cough and occasionally a little fever. Four months after this examination he developed a high temperature and an acute process from which he recovered very slowly. He returned to work in July, 1945. He continued to have slight cough. A year later, in July, 1946, routine examination of the chest was again made (Fig. 8*B*). At this time, however,

he had a chronic cough and some physical findings such as diminished breath sounds and dullness below the right clavicle. Later examination in this hospital revealed a characteristic atelectasis of the same segment of lung which was seen to be emphysematous in the roentgenogram made eighteen months earlier. Planigraphy and bronchography showed a characteristic carcinomatous obstruction of the right upper lobe bronchus which was later confirmed both by bronchoscopy and by exploration. The lesion could not be extirpated. (Case of Dr. R. W. Bray.)

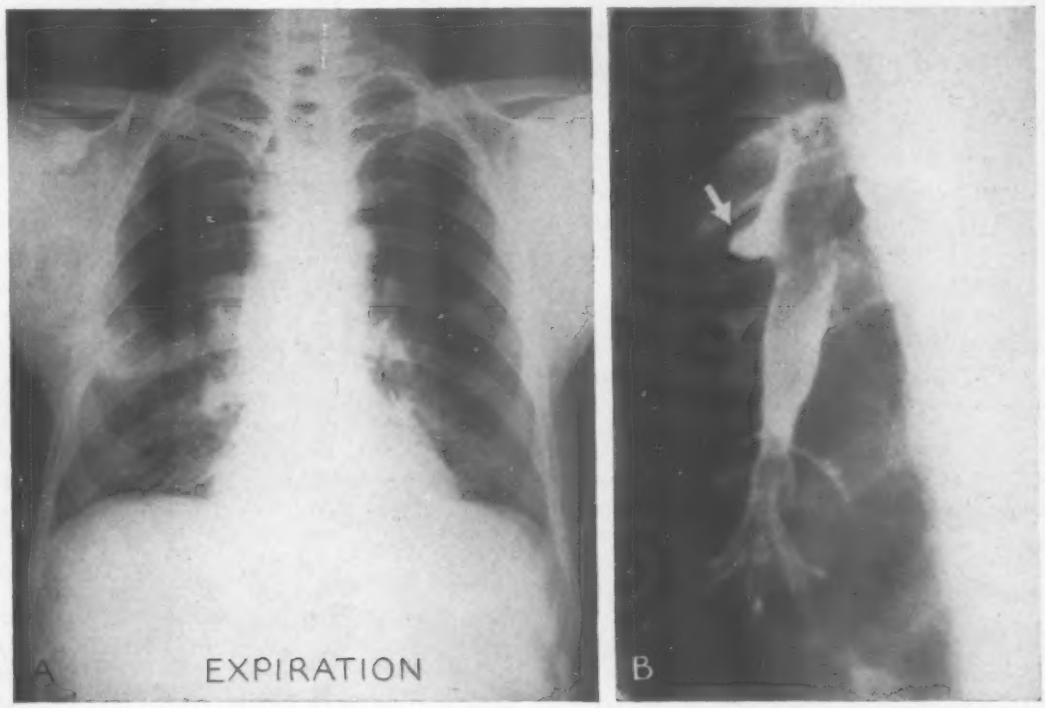

Fig. 7. Case xiii. Bronchogenic carcinoma with obstructive emphysema and atelectasis from the same obstruction. *A*, posteroanterior roentgenogram in expiration. Note the marked radiability of the upper portion of the right upper lobe in contrast to that of the opposite side and especially to the density of the lower portion of the lung. The latter shows the normal change resulting from expiration. In addition, there is a wide band of greatly increased density at the level of the horizontal fissure. The latter is in a low position although the diaphragm is elevated. There is therefore an obstructive emphysema of most of the upper lobe and atelectasis of its inferior portion. *B*, bronchogram made shortly thereafter. The characteristic carcinomatous obstruction of the right upper lobe is well shown (arrow). Note the appearance of complete obstruction despite the emphysema. This is probably owing to the fact that air may get into the lobe during coughing or straining while the viscous oil will not advance through so tiny an opening. The atelectasis below is the result of a more complete closure of that segmental bronchus. Planigrams made at the same time gave an identical picture of the tumor.

Comment. In this case, then, a localized finding suggestive of carcinoma of the bronchus was present approximately two months before the very first symptom and eighteen months before any physical findings or serious symptoms were apparent.

Finally, I should like to report one more case which was somewhat complicated but illustrates again the possibility of early diagnosis of carcinoma of the lung prior to the onset of symptoms.

Case xv. A physician was known to have an enlarged right root shadow with calcification within it for many years. He was in the habit

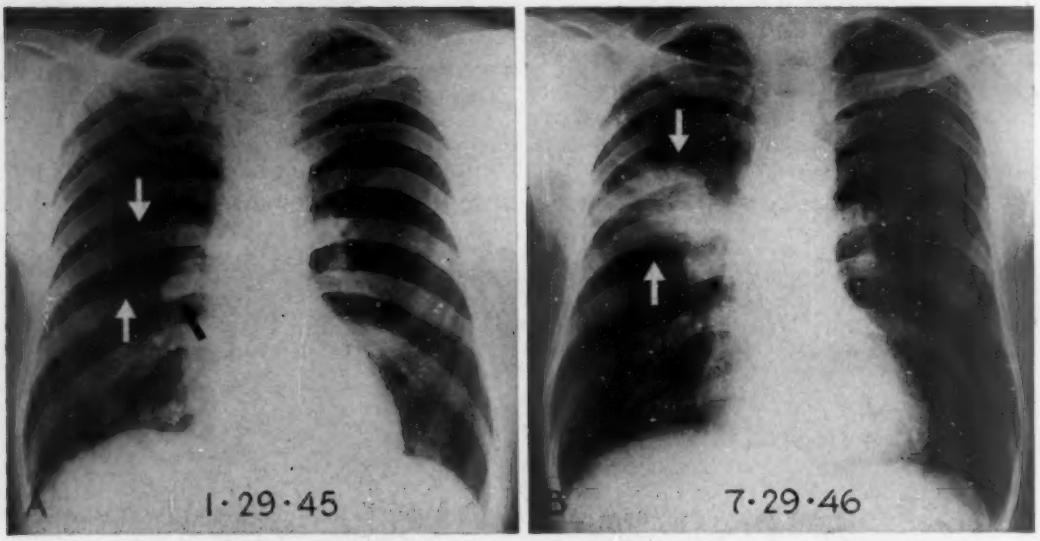

FIG. 8. Case XIV. Bronchogenic carcinoma showing segmental obstructive emphysema for over a year before onset of symptoms. *A*, posteroanterior roentgenogram in deep inspiration made as a routine procedure. Note slight increase in radiability of entire right lung with particular increase in segment of right upper lobe (arrows). There is a slight enlargement of the hilar shadow (arrow) of questionable significance. Roentgenograms made in the expiratory phase at this time would undoubtedly have exhibited the emphysema more effectively. *B*, re-examination eighteen months later, several months after the onset of symptoms. Note dense area of atelectasis (arrows) involving the same segment which was already emphysematous at earlier examination. The hilar shadow is definitely enlarged. (Courtesy of Dr. R. W. Bray.)

of having films of his chest made at yearly intervals because of this finding, although he had no specific symptoms. About two years before the development of any pulmonary symptoms he had a roentgen examination because he had a moderate hypertension and the determination of his heart size was desired. This examination was made at another hospital. A film was made in deep inspiration (Fig. 9*A*) and because the technician thought that this was an error, since the diaphragms were down too far, another film was made in mid respiration (Fig. 9*B*). It is interesting to observe the distinct difference between these two films at a time when this man had no symptoms whatever. There is clearly an obstructive emphysema of the right lung shown only in the expiratory film. He was re-examined approximately a year and a half later in deep inspiration only. At that time the first evidences, in addition to the obstructive emphysema, became apparent; that is, the root shadow had extended farther into the base of the lung and a nodule had appeared along its outer periphery. Unfortunately, because of the fact that the shadow had been large before and comparison was not made between this and the previous films, these findings were not observed. About three months later he coughed up a pea-sized broncholith. Two months later, he developed a dry cough accompanied by weakness, malaise and some dyspnea. Re-examination of the chest May 1, 1947, is illustrated in Figure 9*C*. A characteristic nodular tumor in the right hilum was seen and a diagnosis of carcinoma of the bronchus was made by Dr. J. R. Aurelius. Bronchoscopy on May 15 and May 22 revealed no findings so that the diagnosis was not accepted. About this time a few acid-fast bacilli were found in a smear from the sputum so he was sent to a tuberculosis sanatorium where he remained for some weeks. Finally on July 10, bronchoscopic biopsy revealed an undifferentiated carcinoma. Pneumonectomy was done but metastasis to the cervical lymph nodes was already present and he died some months later.

Comment. Minor changes in the lung indicative of emphysema might have been observed about two years prior to the onset of symptoms. Definite enlargement of the root shadow was present on roentgen

examination five months before the onset of symptoms. Such cases indicate unequivocally that in bronchogenic carcinoma positive roentgen signs may well be present before the first appearance of symptoms.

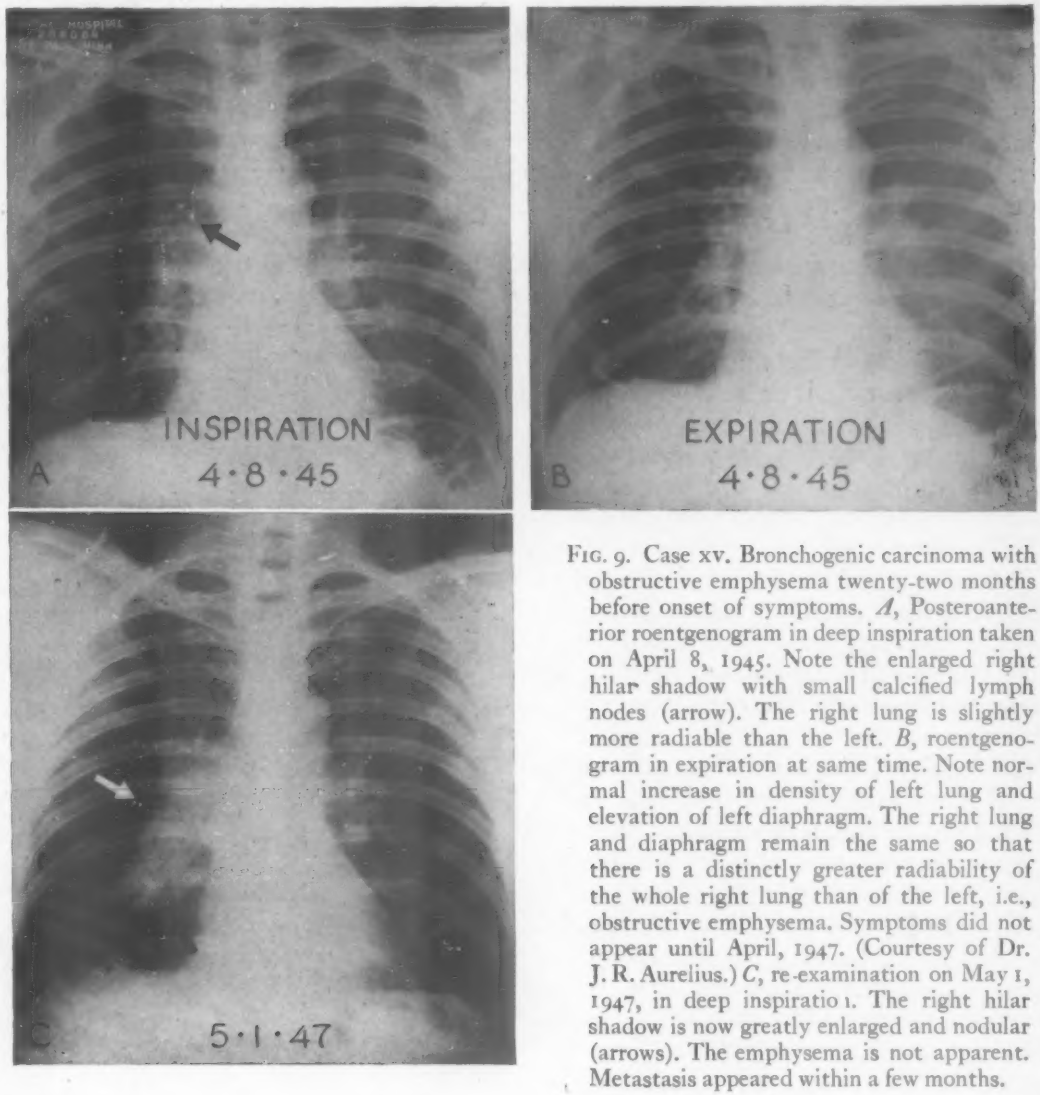

Fig. 9. Case xv. Bronchogenic carcinoma with obstructive emphysema twenty-two months before onset of symptoms. *A*, Posteroanterior roentgenogram in deep inspiration taken on April 8, 1945. Note the enlarged right hilar shadow with small calcified lymph nodes (arrow). The right lung is slightly more radiable than the left. *B*, roentgenogram in expiration at same time. Note normal increase in density of left lung and elevation of left diaphragm. The right lung and diaphragm remain the same so that there is a distinctly greater radiability of the whole right lung than of the left, i.e., obstructive emphysema. Symptoms did not appear until April, 1947. (Courtesy of Dr. J. R. Aurelius.) *C*, re-examination on May 1, 1947, in deep inspiratio 1. The right hilar shadow is now greatly enlarged and nodular (arrows). The emphysema is not apparent. Metastasis appeared within a few months.

SUMMARY

There are definite limitations to the roentgen demonstration of abnormalities. Some of these may be clearly defined and may be expressed in terms of the relationship of the appearance of roentgen signs to the inception of the disease or to the onset of symptoms or in a quantitative way. The possibilities and limitations of roentgen diagnosis are particularly well illustrated in diseases of the thorax. The results of some of our studies in this field are summarized as follows:

1. Pulmonary edema can be detected before the onset of appreciable symptoms and in the very earliest stage of its development, providing it is an intra-alveolar type of process.

2. Interstitial edema is poorly demon-

strated by roentgenologic examination.

3. Pleural effusion in amounts of 100 cubic centimeters or more can be detected if change in position of the patient is utilized during the examination.

4. Bacterial pneumonias are demonstrable, in some cases, within a few hours after the first onset of symptoms and in practically all cases within twelve hours after the first onset.

5. Atypical or virus pneumonias do not give distinctive roentgen manifestations for twenty-four to forty-eight hours after the onset of the symptoms and the extent of the pathologic changes is not well demonstrated.

6. Pulmonary tuberculosis of the ordinary chronic type is demonstrated on the roentgenogram in from ten to twenty weeks after the first exposure to the disease. In almost all cases of parenchymal tuberculosis of the chronic type the roentgen findings precede the symptoms.

7. Miliary tuberculosis gives symptomatic evidence of its presence before the roentgen findings are apparent and symptoms may be present for as long as seven weeks without any roentgen evidence whatever.

8. Nodular lesions such as metastases are demonstrable when their size is 3 millimeters or more in diameter. Miliary metastases may not be seen until they are very numerous or large in size.

9. Bronchogenic carcinoma almost invariably gives positive roentgen signs, if thorough examination is done, when symptoms are present. In many cases of bronchogenic carcinoma, the roentgen findings will be present before the onset of any respiratory symptoms. Examination during expiration as well as inspiration will facilitate the early diagnosis.

Further studies of similar nature should be undertaken to determine the limitations of roentgen examination in the diagnosis of all disease processes.

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THE ROENTGEN FINDINGS IN INTRACRANIAL MASS LESIONS

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THE roentgen diagnosis and localization of intracranial mass lesions has been greatly aided by the introduction of air and other contrast media studies. From conventional film studies alone, many roentgenologists concede that a localizing diagnosis can be made in only 10 to 20 per cent of all cases. In view of this rather disappointing percentage, it was decided to critically review a consecutive series of 123 cases with proved intracranial mass lesions. Cases without adequate roentgenographic studies were omitted.

The roentgenograms of each case were studied simultaneously by both writers. There was no previous knowledge of the operative and pathologic findings, and the roentgen abnormalities were tabulated before the former were reviewed. In this way, it was unlikely that findings would be read into the roentgenograms.

Below is a specimen of the tabulation method employed for each case. For reasons of space economy, tabulation of the entire series has been omitted from this report.

Case	Age	Conventional Film Findings	Conventional Film Diagnosis	Air and Special Studies	Final Roentgen Diagnosis	Operative and Pathologic Findings
29	64m	Erosion of superior and posterior portions of the right petrous pyramid. Pineal calcified and shifted 10 mm. to the left. Normal acoustic meati (Stenvers)	Right cerebellopontine angle tumor	None	Right cerebellopontine angle	Large tumor arising from 8th nerve at cerebellopontine angle on the right. Histopathology perineurial fibroblastoma

Routine views of the skull consisted of a posteroanterior, an occipital view, and stereoscopic projections of both lateral positions. Where indicated, oblique views of the mastoids and petrous pyramids (Stenvers) and optic foramina views were obtained.

STATISTICAL FINDINGS

Table 1 indicates the histopathologic distribution of the lesions in this series. The incidence percentage does not deviate significantly from many published series.[1,2] Gliomas comprised 33.3 per cent and meningiomas 20.3 per cent of all lesions. Pituitary tumors were considerably less frequent (4.9 per cent) than in other reports, because eosinophilic adenomas were given roentgen therapy without surgery, and hence do not appear in our series.

About 50 per cent of the lesions were in individuals past forty years, with 44 per cent in patients between forty and sixty years (Table 1). The average age incidence of some of the more common lesions was:

Metastatic cancer	50 years
Meningioma	46 years
Glioblastoma multiforme	43 years
Craniopharyngioma	29 years
Astrocytoma	25 years
Medulloblastoma	6 years

In Table 11 is given the anatomic distribution of the lesions and also the age incidence. About 50 per cent were in the cerebral hemispheres, and these were mostly in patients between the ages of

TABLE I

Histopathologic Type	Age Incidence (years)								Total	Per cent
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80		
Glioblastoma multiforme	1	—	4	2	4	5	—	2	18	14.6
Astrocytoma	2	5	3	1	3	1	—	—	15	12.2
Ependymoma	1	—	—	2	—	—	—	—	3	2.4
Astroblastoma	—	—	—	—	1	1	—	—	2	1.6
Medulloblastoma	2	—	—	—	—	—	—	—	2	1.6
Oligodendroglioma	—	—	1	—	—	—	—	—	1	0.8
TOTAL GLIOMAS									(41)	(33.3)
Meningioma	—	3	—	6	8	8	—	—	25	20.3
Perineural fibroblastoma	—	—	2	2	3	1	1	—	9	7.3
Aneurysm, circle of Willis	—	1	1	1	1	1	2	—	7	5.7
Aneurysm, arteriovenous	—	—	—	1	—	—	—	—	1	0.8
Chromophobe adenoma	—	—	1	—	2	3	—	—	6	4.9
Metastatic malignancy	—	—	—	—	3	3	—	—	6	4.9
Abscess	1	3	—	—	—	—	—	—	4	3.2
Craniopharyngioma	1	—	2	—	—	1	—	—	4	3.2
Dermoid and epidermoid cyst	2	—	3	—	—	—	—	—	5	4.0
Colloid cyst	—	1	—	—	1	1	—	—	3	2.4
Subdural hematoma	—	1	—	1	—	1	—	—	3	2.4
Hemangioma	—	—	—	2	1	—	—	1	4	3.2
Chordoma	—	—	—	—	—	1	—	—	1	0.8
Hemangioblastoma	—	1	—	—	—	—	—	—	1	0.8
Retinoblastoma	1	—	—	—	—	—	—	—	1	0.8
No histopathology	—	1	—	—	—	1	—	—	2	1.6
TOTAL	11	16	17	18	27	28	3	3	123	
PERCENTAGE	8.9	13.0	13.8	14.6	21.9	22.7	2.4	2.4		

TABLE II

Location of Lesion	Age Distribution								Total
	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	
Cerebral hemispheres	3	8	7	9	15	17	—	3	62
Deep toward midline					2	2			4
Supratentorial midline	1	2	4	2	2	4	—	—	15
Cerebellar	5	5	—	2	—	—	—	—	12
Other infratentorial	—	—	—	1	1	—	—	—	2
Pituitary	—	—	1	—	2	3	—	—	6
Orbit	3	—	1	—	—	—	—	—	4
Aneurysms at base	—	1	1	2	1	1	2	—	8
Cerebellopontine angle	—	—	2	2	3	1	1	—	9
Arising from paranasal sinuses	—	—	1	—	—	—	—	—	1

forty and sixty years. Infratentorial lesions made up 18.7 per cent, occurring mainly in individuals below the age of twenty.

The high percentage of cases where localization could be made on conventional film studies came as a considerable surprise to us. Table III illustrates the diagnostic efficacy of conventional film studies and also of additional air studies. From roentgenograms made without contrast media,

a localizing diagnosis was made in about 50 per cent of all cases. A high percentage of localization is not surprising in pituitary tumors or in dermoid and epidermoid cysts because of their characteristic destructive effect on the bony structures. Of the 9 cerebellopontine angle lesions, diagnosis was made in 8. This high percentage is largely due to the changes seen on oblique views of the pyramids, where enlargement of the porus acusticus can be seen. Of the 25 meningiomas, 16 were localized on the routine films. Of these only 8 showed tumor calcification or bone sclerosis. Dyke[4] found that about 50 per cent of meningiomas produced localizing changes on the roentgenogram. Infratentorial lesions generally could not be accurately localized on conventional roentgenograms. Commonly there was indirect evidence of increased intracranial pressure.

A word about localization. While usually the localization could be made with considerable accuracy, in cases where only a pineal shift was found, obviously we could indicate the side of the lesion, but no more. This was deemed sufficient to include with other cases localized by conventional films.

Lesions were suspected in 18 (14.5 per cent) cases. The roentgen findings in this group consisted mainly of evidence of increased intracranial pressure, widened sutures, increased convolutonal markings, and erosion or marked demineralization of the dorsum sellae.

In only 44 patients (35.8 per cent) were the conventional films completely negative. Thus, there were either definite localizing findings or suspicion of an expanding intracranial lesion in 64.1 per cent of all the conventional roentgen examinations.

Air studies were done on 50 patients. Of

TABLE III

Histopathologic Type	Total	Conventional Films. Conclusions			Air Studies Done	Localization Made from Air Studies Where Conventional Films Failed to Localize
		Localization Made	Tumor Suspected	Negative		
Meningioma	25	15	3	7	13	6
Glioblastoma multiforme	18	7	4	7	11	7
Astrocytoma	15	5	5	5	8	5
Other gliomas	8	1	4	3	1	1
Pituitary tumors	6	6	—	—	—	—
Perineural fibroblastoma	9	8	—	1	—	—
Aneurysm	8	4	—	4	4	2*
Craniopharyngioma	4	3	—	1	—	—
Colloid cyst	3	—	1	2	3	3
Metastatic carcinoma	6	2	—	4	4	3
Abscess	4	—	1	3	1	1
Dermoid and epidermoid cyst	5	4	—	1	—	—
Subdural hematoma	3	2	—	1	2	1
Hemangioma	4	2	—	2	2	1
Chordoma	1	1	—	—	—	—
Hemangioblastoma	1	—	—	1	—	—
Retinoblastoma	1	—	—	1	—	—
No histopathology	2	1	—	1	1	—
	123	61 49.6%	18 14.5%	44 35.8%	50 40.7%	30 24.4%

* Cisterna chiasmatis failed to fill.

TABLE IV

Location	No. Cases	Sellar Erosions and Deformities	Demineralization of Dorsum	Widened Sutures	Increased Digital Markings	Calcification	Table Changes	Sphenoidal Fissure Changes	Petrous Pyramid Erosions	Pineal Displacement	Choroid Displacement	Orbital Bone Changes	Enlarged Internal Auditory Meatus	Displaced Falx	Increased Table Vascularity	
Frontal and frontoparietal	37	1	6	1	1	4	7	—	—	8	—	2	—	—	1	Depressed Cribriform Plate 1
Posterior parietal and occipital	7	2	1	—	1	2	1	1	—	1	1	—	—	—	—	
Temporal	13	—	2	1	1	3	1	3	1	2	1	—	—	1	—	
Intrasellar	6	6	—	—	—	—	—	1	—	—	—	—	—	—	—	
Suprasellar and parasellar	21	6	—	1	—	4	—	4	1	3	—	2	—	—	—	
Deep-seated near midline	3	—	1	—	—	—	—	—	—	—	—	—	—	—	—	
Midline and ventricular	12	3	1	4	3	1	—	—	—	—	—	—	—	—	—	
Orbital	4	—	—	—	—	—	—	1	—	—	—	3	—	—	—	
Cerebellar	10	—	3	7	7	—	—	—	—	—	—	—	—	—	—	
Cerebellopontine	10	1	1	—	—	1	—	—	3	3	—	—	6	—	—	
TOTAL	123	19	15	14	13	15	9	10	5	17	2	7	6	1	1	
PERCENTAGE		15.5	12.2	11.4	10.6	12.2	7.3	8.1	4.05	13.8	1.6	5.7	4.8	0.8	0.8	

TABLE V

Histopathology	No. Cases	Sellar Changes	Calcification	Suture Widening	Pyramid Changes	Sphenoidal Fissure Changes	Increased Table Vascularity	Table Changes	Pineal Displacement	Localized Hyperostosis
Meningioma	25	7	3	—	2	4	—	5	5	5
Glioblastoma multiforme	18	6	—	2	—	1	—	—	5	—
Astrocytoma	15	4	4	5	—	1	—	—	—	—
Other gliomas	8	2	1	2	—	—	—	1	—	—
Pituitary tumors	6	6	—	—	—	1	—	—	—	—
Perineural fibroblastoma	9	2	1	—	7	—	—	—	2	—
Aneurysms	8	1	2	—	—	1	—	—	—	—
Craniopharyngioma	4	2	3	1	—	—	—	—	—	—
Colloid cyst	3	1	—	—	—	—	—	—	—	—
Metastatic carcinoma	6	—	—	—	—	—	—	—	2	—
Abscess	4	—	—	2	—	—	—	—	—	—
Dermoid and epidermoid	5	—	—	—	—	1	—	1	—	—
Subdural hematoma	3	—	—	—	—	—	—	1	2	—
Hemangioma	4	2	—	—	—	—	1	1	—	—
Chordoma	1	1	1	—	—	1	—	—	1	—
Hemangioblastoma	1	—	—	1	—	—	—	—	—	—
Retinoblastoma	1	—	—	—	—	—	—	—	—	—
No histopathology	2	—	—	1	—	—	—	—	—	—
TOTAL	123	34	15	14	9	10	1	9	17	5
PERCENTAGE		27.7	12.2	11.4	7.3	8.1	0.8	7.3	13.8	4.1

these, only 2 were negative in the presence of a proved tumor. One was a meningioma in the occipital region near the midline. With air studies, localizing diagnosis was made in 30 cases where the conventional film findings were negative or indeterminate. A total of 74.0 per cent of all the intracranial lesions were thus localized by routine film studies and/or air studies. Many patients, however, in spite of negative findings on the routine film studies, did not have air studies because of clearcut clinical localizing symptoms. This was particularly true of children with cerebellar lesions.

Tables IV and V are statistical compilations of the abnormal roentgen findings in all the cases of this series. The roentgen findings are correlated with the location of the lesion (Table IV) and with the histopathologic diagnosis (Table V).

Sella Turcica. Changes in the sella turcica were the most common abnormal roentgen finding in the series, occurring in 34 cases (27.6 per cent). Characteristic sellar changes were found in practically all the pituitary tumors, i.e., ballooning of the sella, erosion or thinning of the posterior clinoids and dorsum, and sharpening of the anterior clinoids. In one case, however, the dorsum was destroyed, but the rest of the sella was intact. This could not be distinguished roentgenologically from increased intracranial pressure with erosion of the dorsum (Fig. 2). In suprasellar and parasellar lesions, pressure erosions of the dorsum or floor of the sella were seen in 6 of the 21 cases. In extrasellar tumors, where no direct pressure could be exerted against this structure, the changes in the dorsum are usually the result of the increased intra-

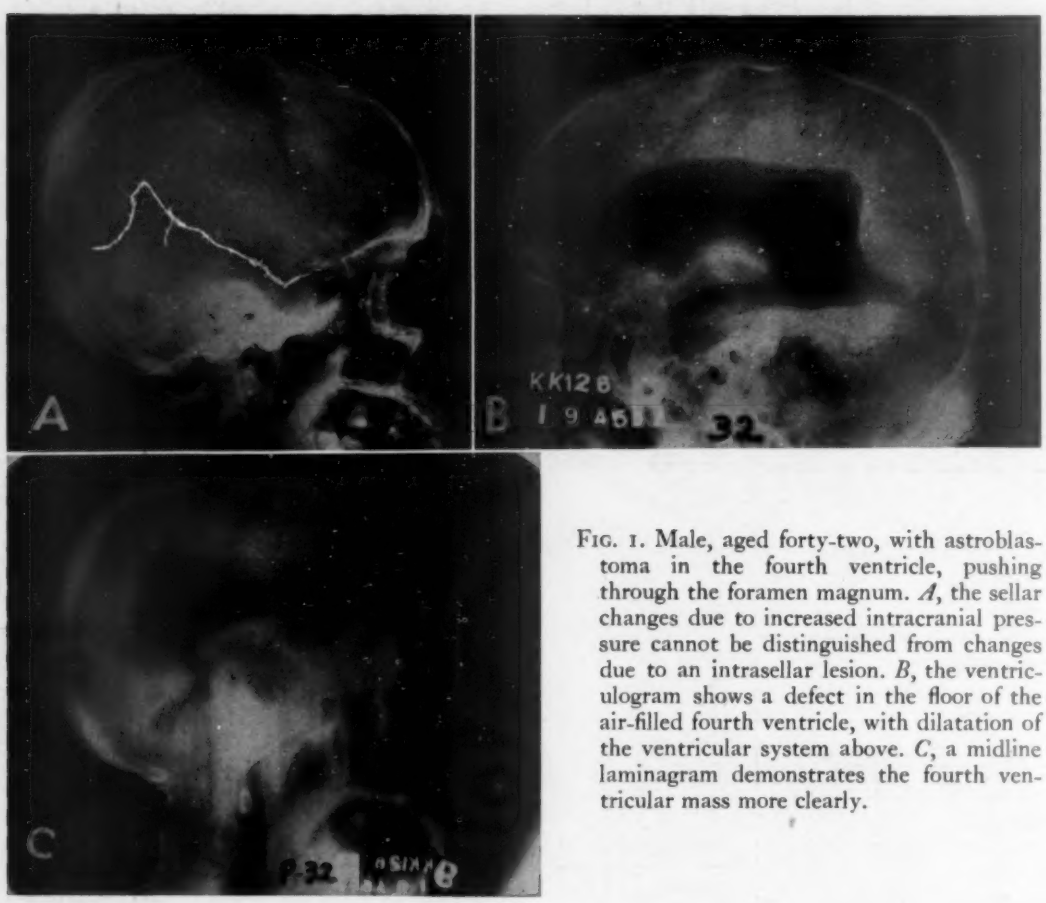

FIG. 1. Male, aged forty-two, with astroblastoma in the fourth ventricle, pushing through the foramen magnum. *A*, the sellar changes due to increased intracranial pressure cannot be distinguished from changes due to an intrasellar lesion. *B*, the ventriculogram shows a defect in the floor of the air-filled fourth ventricle, with dilatation of the ventricular system above. *C*, a midline laminagram demonstrates the fourth ventricular mass more clearly.

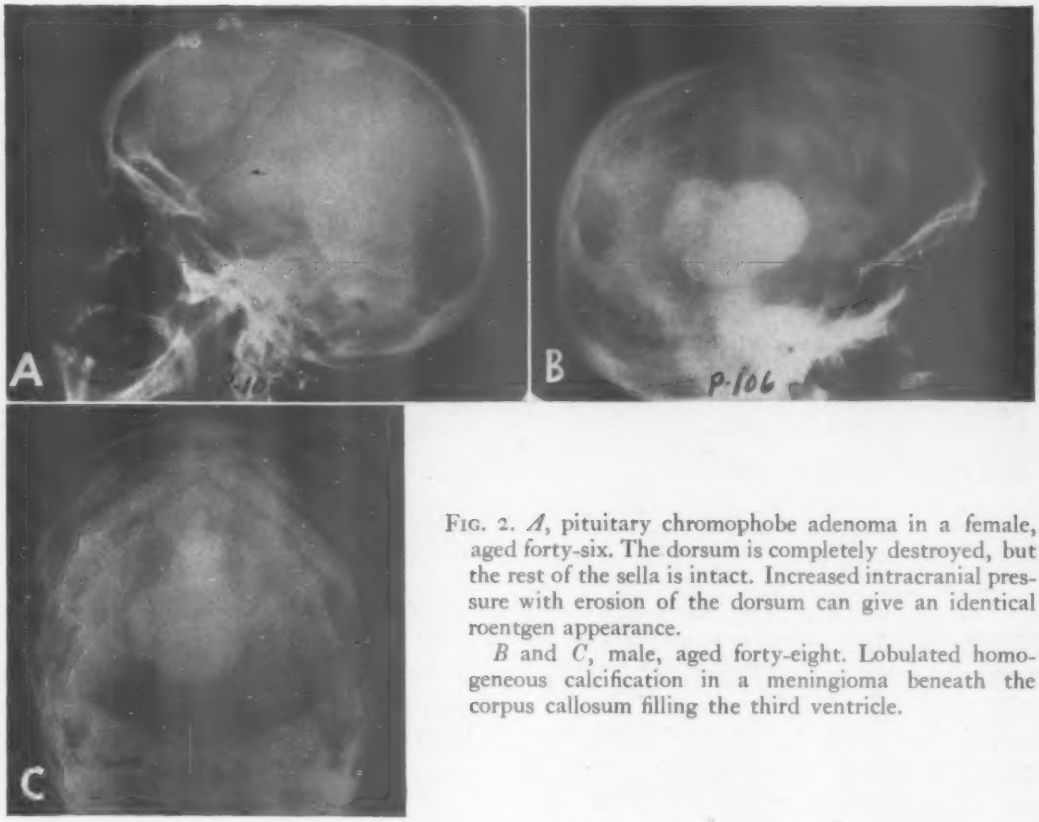

Fig. 2. *A*, pituitary chromophobe adenoma in a female, aged forty-six. The dorsum is completely destroyed, but the rest of the sella is intact. Increased intracranial pressure with erosion of the dorsum can give an identical roentgen appearance.

B and *C*, male, aged forty-eight. Lobulated homogeneous calcification in a meningioma beneath the corpus callosum filling the third ventricle.

cranial pressure where the dilated third ventricle was pulsating against the dorsum. However, this may closely simulate a suprasellar or even an intrasellar lesion (Fig. 1). It may be extremely difficult if not impossible to distinguish dorsum erosion from demineralization. Of the 34 cases with sellar changes, we considered 15 to be demineralization only.

Calcifications. In 16.3 per cent of the

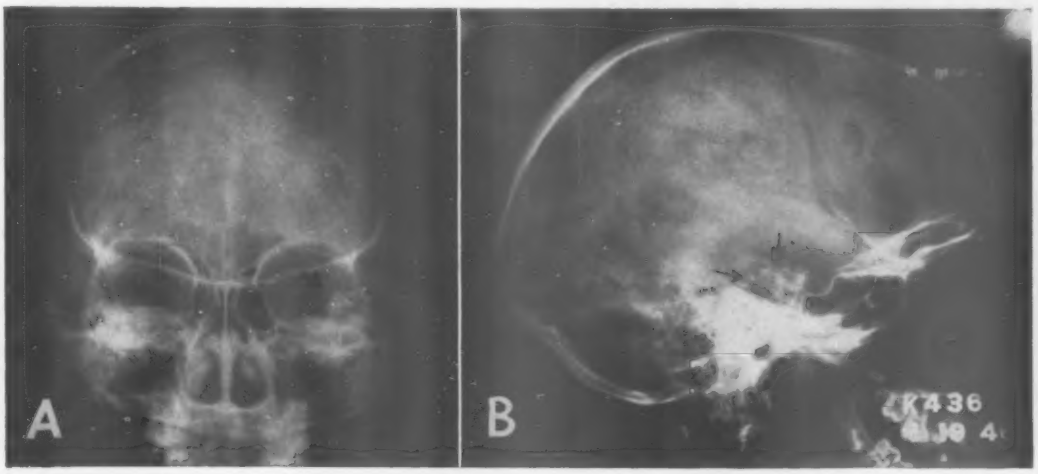

Fig. 3, *A* and *B*. Female, aged eleven. Astrocytoma of the left temporal lobe with amorphous calcification.

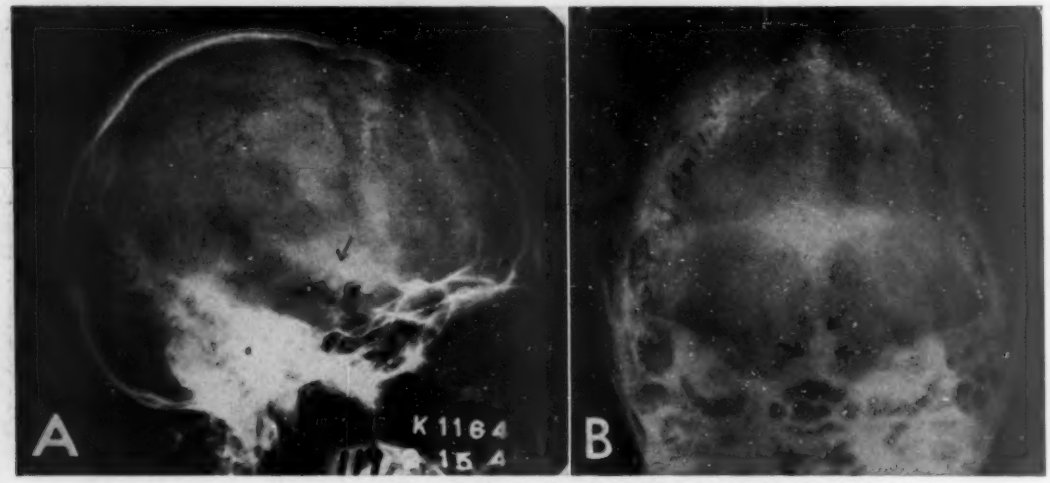

FIG. 4, *A* and *B*. Male, aged twenty-eight. Irregular calcification above the sella in a craniopharyngioma.

cases there was calcification within the lesion or a sclerotic bone reaction in the immediate vicinity (Table v). These changes were seen in about one-third of the meningiomas (Fig. 2*A*). In these latter tumors, localized hyperostosis occurred more often than amorphous calcification. Characteristic spicule formation in the tables was seen only once in the 25 cases of meningioma. About one-fourth of the astrocytomas showed calcification, usually of the fine granular variety (Fig. 3). Of the 4 craniopharyngiomas, 2 showed the characteristic calcification in the midline above the sella (Fig. 4). Thin crescentic calcification appeared in 2 of the 8 aneurysms (Fig. 5). The single oligodendroglioma of the series was heavily calcified (Fig. 6). Not one of the 18 glioblastomas was calcified, and only one of the less common gliomas showed calcium deposits.

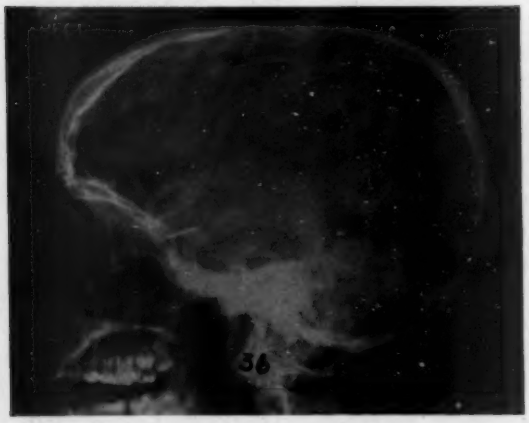

FIG. 5. Male, aged eighteen. The thin crescentic calcification in the right occipitoparietal area near the midline was within the wall of a large arteriovenous aneurysm between the posterior cerebellar artery and the vein of Galen. Note the roentgen evidence of increased intracranial pressure.

Suture Separation and Increased Digital Markings. Widening of the sutures was observed in 14 cases. Half of these were in cerebellar lesions, and 5 others in midline or intraventricular lesions, with internal block hydrocephalus (Fig. 7 and 14). In only 2 cases were widened sutures observed in hemispheric lesions. The average age for suture separation was ten years. In older individuals with firmer sutures, long-standing internal hydrocephalus and increased intracranial pressure was more apt to produce exaggerated convolutional markings and demineralization of the dorsum sellae.

Increased convolutional markings were observed in 13 cases. It is extremely difficult if not impossible to consider the markings definitely exaggerated unless these findings are quite advanced. There is too great a variation in convolutional markings

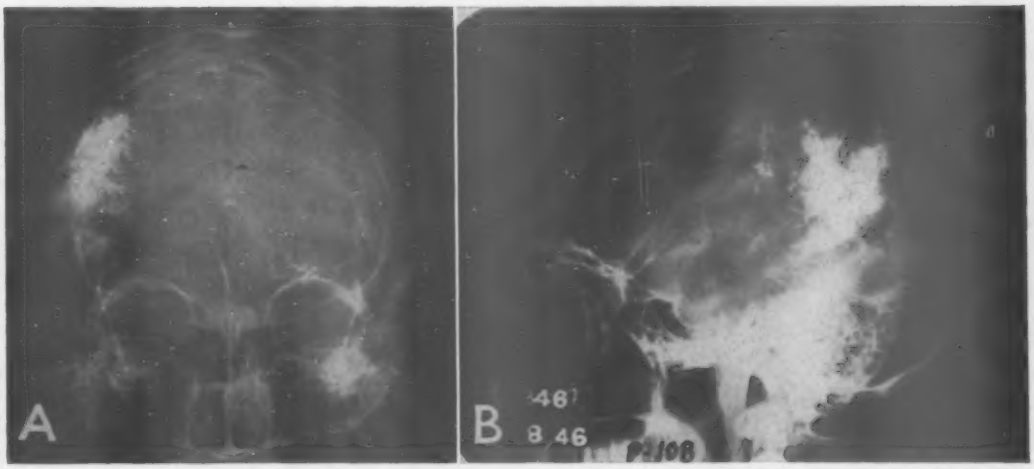

Fig. 6, *A* and *B*. Male, aged twenty-eight. Oligodendroglioma arising from the right temporal lobe with extensive amorphous calcification in the tumor.

in normal skulls, and technical factors which change film contrast make decided variations in these markings even in the same skull. Over half the cases with definitely increased markings had cerebellar lesions.

Petrous Pyramid Changes. Abnormalities of the petrous pyramids from pressure erosion or invasion were seen in 9 cases (7.3 per cent), Of special interest are the findings in 9 cases of perineural fibroblastoma of the eighth nerve. In 3 cases, definite erosion of the superior and posterior margins of the pyramid was apparent. In 4 cases, without definite pyramid erosion, roentgenograms taken in Stenvers' position showed one internal acoustic meatus definitely enlarged (Fig. 8 and 9). This was not apparent on posteroanterior or occipital views. As a control, 35 patients without cerebellopontine angle signs or symptoms were studied with Stenvers views of the pyramids. In almost all these cases, the internal auditory meati were clearly seen, and there was no significant difference in size of the left and right meati. This com-

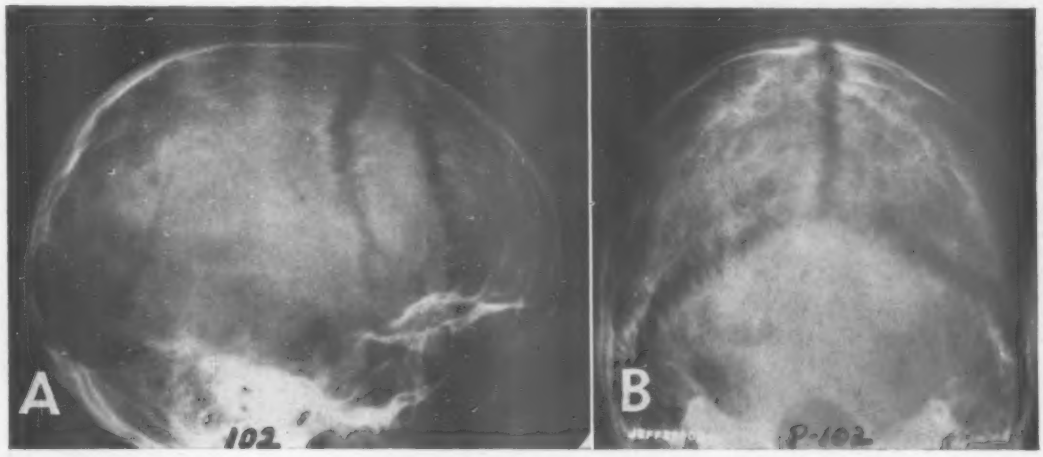

Fig. 7, *A* and *B*. Male, aged fourteen. Widened sutures and increased digital markings from increased intracranial pressure. Hemangioblastoma of the left cerebellar hemisphere.

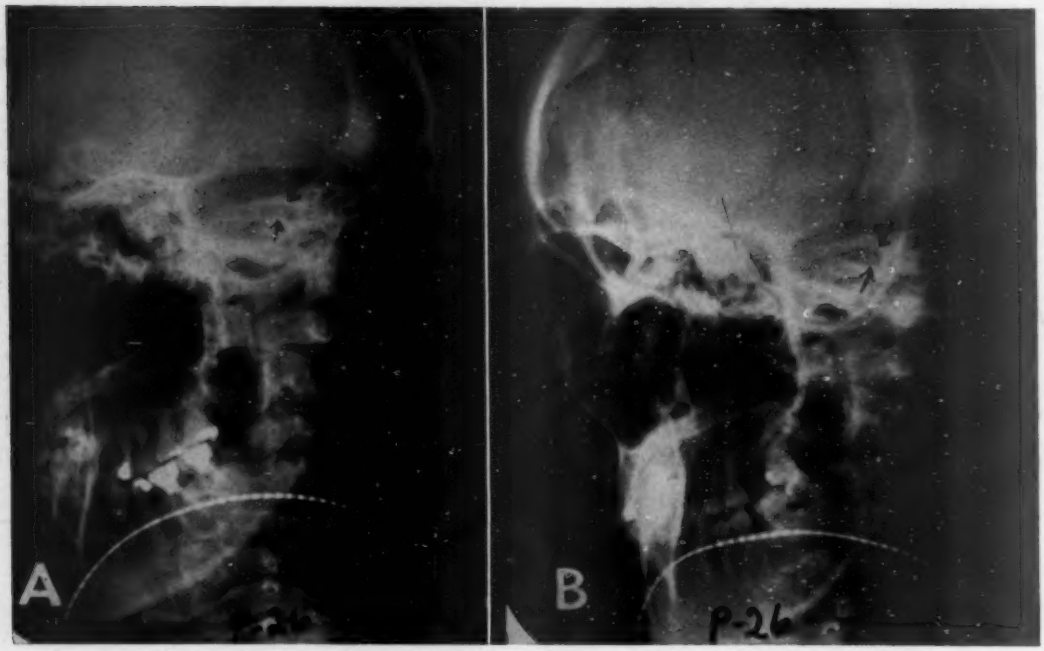

FIG. 8, *A* and *B*. Female, aged twenty-five. Stenvers views of the pyramids showing widened left porus acusticus from perineural fibroblastoma arising from the left eighth nerve. *B* is the left side.

FIG. 9, *A* and *B*. Female, aged thirty-eight. Perineural fibroblastoma arising from the left eighth nerve. *B* shows the widened left porus acusticus compared to the right (*A*).

plete symmetry of normal internal auditory meati proves that enlargement of one meatus in a patient with suspected angle lesion is of great diagnostic significance. The oblique Stenvers view therefore becomes an indispensable aid in the roentgen diagnosis of angle lesions. In one case of acoustic neuroma, there was the most unusual finding of a ring-like calcification behind the pyramid, due to calcification of the rim of the tumor (Fig. 10). In only one of these cases were the roentgen findings completely negative, but no Stenvers views were made in this patient, preoperatively.

Sphenoid Bone Changes. Changes in the sphenoid wings and fissures were found in 10 cases (0.8 per cent). Of these, 4 were from local tumor pressure. In 3 cases, temporal lobe lesions, with swelling and edema of the temporal lobe, led to pressure demineralization of the homolateral sphenoid wings. A unilateral hemispheric tumor, with increased pressure unilaterally, can also produce this unilateral demineralization of the sphenoid wings (2 cases). Meningiomas are the most common lesion directly involving the wings. Bone erosion or hyperostosis or even both may result. Asymmetry of the fissures without bony involvement cannot be considered of diagnostic significance.

Fig. 10. Male, aged fifty-five. Perineural fibroblastoma just behind the right internal auditory meatus. The ring-like calcification within the tumor is most unusual in this type of lesion.

Fig. 11. Female, aged thirty-four. The numerous wide vascular channels in the frontal bone at the vault were due to a meningeal hemangioma attached to the left side of the longitudinal sinus.

Erosions of the Tables. Erosions of the tables of the skull indicate a mass against or within the bone. Of the 9 cases with erosion of the tables, 5 were meningiomas. An epidermoid and hemangioma accounted for 2 others.

Enlargement of the vascular channels in the calvarium proved to be an uncommon and inaccurate roentgen sign of an intracranial lesion. There is too great a normal variation in size and number of vascular channels, often with unilateral preponderance. However, in one of our cases (Fig. 11), there was a collection of very large channels due to a meningeal hemangioma. While not to be overlooked, unusual vascular channels do not constitute a dependable localizing roentgen sign.

Lateral Pineal Shifts. A lateral shift of the calcified pineal body, in our opinion, is one

of the most important findings to be searched for in cases of suspected intracranial mass lesions. We feel its importance has not been sufficiently emphasized in the past.

In our series, the pineal body was calcified in 27.6 per cent. The average age of patients with calcified pineal was 48.3 years, with the youngest in a girl aged thirteen. Pineal calcification is known to increase in the older age groups.

TABLE VI

PINEAL DATA

Pineal Calcifications—35
Lateral Shift —17
Backward Shift — 1 (sphenoid meningioma)

	Location of Lesion	Pineal Lateral Shift	Pineal Seen No Shift
	Cerebellopontine	3	2
	Hemisphere (cerebral)	10	3
	Middle fossa	2	2
	Subdural hematoma	2	—
	Carotid aneurysm	—	2
	Suprasellar	—	3
	Intrasellar	—	3
	Orbital	—	1
	Cerebellar	—	1
	TOTAL	17	17

Millimeters of Lateral Shift (Difference between the 2 measurements to right and left outer tables): 15, 13, 13, 13, 10, 10, 10, 10, 9, 9, 9, 5, 5, 5, 4, 4, 4,

Average shift = 8.8 mm.
Cases where shifted pineal only roentgen finding 11

Of the 35 cases with a calcified pineal, in 17 there was a significant lateral displacement. Table VI gives full information of the degree of shift and location of the underlying lesion.

The technique of measuring for pineal shift is extremely simple. Measurement is made from the midportion of the calcification directly lateral to the outer table of each side. A difference of 4 mm. or more between the two measurements is considered significant of pineal displacement. While it is important for the head to be well centered on the anteroposterior view (pineal best seen on the anteroposterior rather than on the posteroanterior view), rotation up to 10 or 15° does not significantly alter the measurements. We measured many normal cases in poorly centered anteroposterior views, but found no measurement difference greater than 3 mm. unless there was over 15° rotation. In our series there were shifts as great as 15 mm., with an average of 8.8 mm.

A word about identification of the calcified pineal body. Not rarely, the pineal is seen on the lateral view, but on anteroposterior projection it cannot be identified, or it may be confused with a portion of calcified falx, or bony condensation in the occipital bone. In this situation, a stereoscopic pair in the anteroposterior projection will make certain identification of the pineal possible.

Table VI indicates that cerebral hemispheric tumors are most apt to produce lateral pineal shifts. Of the 17 displaced pineals, 10 were from hemispheric tumors, and 2 from subdural hematomas over the hemispheres. In only 3 cases were calcified pineals not displaced by hemispheric mass lesions. Lesions around the midline, base, or beneath the tentorium rarely lead to lateral pineal shift. In 11 cases, the pineal displacement was the *only* roentgen finding, while in 6 cases there were other localizing roentgen findings. It is interesting that 3 of the 10 cases with angle tumors showed lateral pineal shift.

Most investigators have shown more interest in sagittal displacements of the pineal, for which many ingenious measuring devices and methods have been presented.[3,5,7] From our experience, lateral shifts are not only more common but easier

to determine accurately, even when slight. Although a number of cases with lateral shift also showed pineal shift in the sagittal plane, in only one instance was there a definite backward displacement without lateral deviation. This was in a patient with a basisphenoid meningioma.

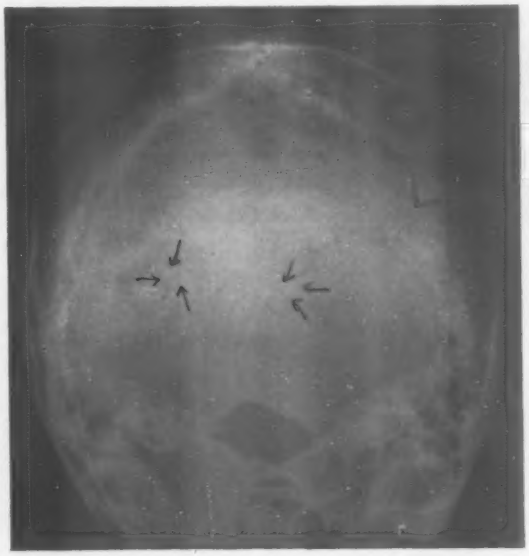

Fig. 12. Male, aged fifty-two. The calcified choroid plexus on the left is displaced considerably to the right by metastatic carcinoma invading the left parietal lobe.

It must be borne in mind that a displacement of the pineal to one side means a probable mass lesion on the other side only when tumor or mass is suspected. Cerebral atrophy, scarring or agenesis will usually pull the pineal toward the affected side.

Fig. 13. Female, aged forty-three. Meningioma of the frontal lobes. This tumor was adherent to the cribriform plate. Note the irregular, uneven cribriform plate.

Displacement of the calcified choroid plexus is a rather unusual finding[4,6] (Fig. 12). It was seen in 2 cases of the series, both in patients with cerebral hemispheric tumor. In one, there was also a pineal shift

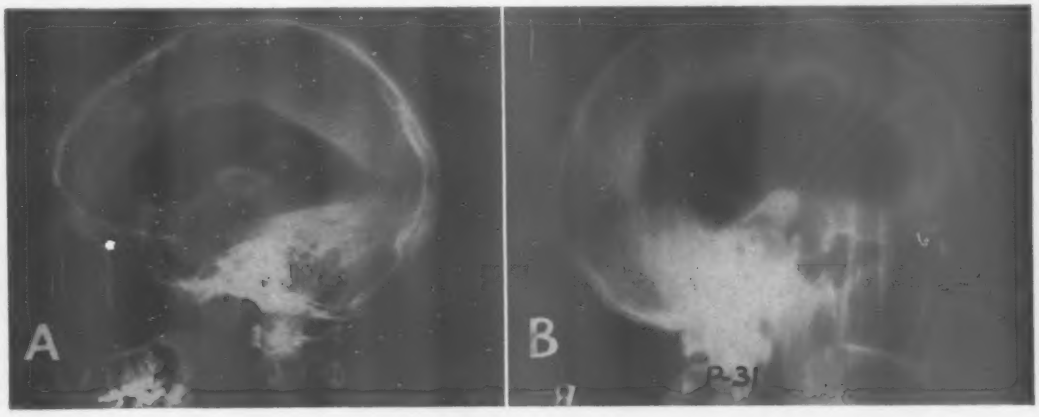

Fig. 14. Two cases of colloid cyst of the third ventricle. *A*, female, aged twenty. Defect in the posterior portion of third ventricle with dilatation of the third and lateral ventricles. *B*, male, aged fifty-eight. A midline laminagram clearly demonstrates the smooth mass in the third ventricle.

to corroborate the diagnosis, but in the other the displacement of the calcified choroid was the sole roentgen finding upon which a diagnosis could be made.

A displacement of the calcified falx was found in a patient with a temporal lobe tumor. This was the only clue to the roentgen diagnosis.

In a case of frontal lobe meningioma, adherent to the cribriform plate, there was a detectable deformity of the plate on the posteroanterior view (Fig. 13).

SUMMARY

1. Roentgen, pathologic and anatomic correlations were made in 123 proved cases of intracranial mass lesions.

2. With routine conventional film studies alone, 49.6 per cent of these cases were localized. With routine roentgenograms and air studies, 74.4 per cent localization was obtained. Only 35.8 per cent of the cases were completely negative on routine skull roentgenograms.

3. Changes in the sella turcica occurred in 27.6 per cent. Intrasellar and extrasellar lesions usually gave characteristically different roentgen changes in the sellar area.

4. Tumor calcification was seen in 12.2 per cent. Meningiomas, astrocytomas, craniopharyngiomas and aneurysms calcified more often than other lesions. Bone sclerosis occurred in 4.0 per cent, from meningioma in all cases.

5. In 11.4 per cent there were widened sutures. This was most common in children with cerebellar lesions.

6. Petrous pyramid erosion and/or widening of the internal auditory meatus were found in 7 of 9 patients with acoustic perineural fibroblastoma. Stenvers views are important for detection of meatal enlargement.

7. Sphenoidal fissure or wing changes were seen in 8.1 per cent. A swollen temporal lobe from local lesion or from generalized increased intracranial pressure may cause demineralization of the sphenoidal wings.

8. The pineal was calcified in 27.6 per cent. About 50 per cent of these showed a significant lateral displacement. Most mass lesions in the hemispheres will displace the pineal to the opposite side. More attention seems warranted to the lateral shift of the pineal than to displacement in the sagittal plane.

We wish to express our sincere gratitude and thanks to Dr. Paul C. Swenson, Professor of Radiology, and to Dr. Rudolph Jaeger, Professor of Neurosurgery, for their cooperation and kindness in making the clinical and roentgen material available to us.

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COMPLETE BLOCK OF THE LUMBAR SPINAL CANAL DUE TO HERNIATION OF THE NUCLEUS PULPOSUS*

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COMPLETE obstruction of the spinal canal by protrusion of the nucleus pulposus of the lumbar intervertebral discs is infrequent. The cases reported up to the present time have been associated with severe symptoms referable to compression of the cauda equina, and in many the differential diagnosis between tumor of the cauda equina and herniated disc could not be made. A review of 150 lumbar myelograms done during the past five years disclosed 5 patients with complete spinal canal block. Four of these had little to suggest compression of the cauda equina, while in the fifth the clinical diagnosis was a cauda equina tumor.

The purpose of this report is to show that complete lower spinal canal block may occur without the signs of cauda equina compression. This can be diagnosed only with pantopaque myelography. In addition, a variation in myelographic technique to outline the superior and inferior margins of the obstructive lesion is described.

CASE REPORTS

CASE 1. M. R. (Hosp. No. 292293), male, aged fifty-nine, first complained of low back pain twenty-one months before admission following mild exercise. This persisted for a few days and then radiated down the posterior aspect of his left leg. It disappeared and recurred intermittently with varying intensity on several occasions apparently without cause. When the pain was most intense he was completely incapacitated. On several occasions he noted numbness in his left foot and the outer aspect of his right thigh. Some aggravation of pain occurred on straining. He did not respond to conservative orthopedic treatment.

Examination showed that his left calf was atrophied 0.5 cm. The ankle jerks were absent bilaterally. Sensory responses and motor power were normal.

Plain roentgenographic examination of the lumbosacral spine on several occasions showed osteoarthritic changes in the lower lumbar vertebrae and narrowing of the lumbosacral interspace.

Myelography after the instillation of 3 cc. of pantopaque between the third and fourth lumbar vertebrae showed an abrupt transverse block about 1 cm. above the inferior margin of the fourth lumbar vertebra when the patient was in the erect position. Small dentate irregularities were present at the caudal end of the pantopaque column. Within the column was a radiolucent streak parallel to the long axis of

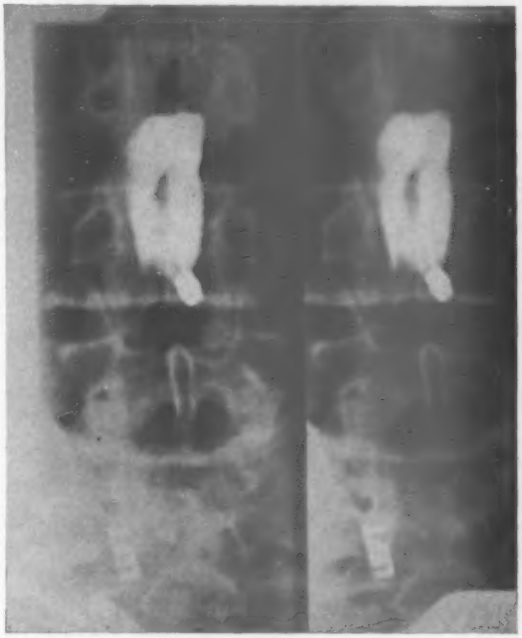

FIG. 1. Case 1. Spot roentgenogram with patient in erect position shows a transverse block above the level of the inferior margin of the fourth lumbar vertebra with dentate serrations of the distal end of the pantopaque column. In the middle of the pantopaque column is a linear radiolucent shadow which at operation was found to be due to edematous nerve roots.

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the spinal canal indicative of a swollen nerve root.

The spinal fluid proteins were 100 mg. per 100 cc.

Preoperative diagnoses ran the gamut from psychoneurosis to cauda equina tumor.

A laminectomy of the fourth and fifth lumbar vertebrae was performed and extradural exploration did not disclose the cause of the block. Intradural exploration at first failed to reveal a mass, but the roots of the cauda equina were markedly swollen. Finally the protruded disc was divulged as a bulge in the midline anteriorly and removed through a transdural incision. The disc was large, measuring more than 4 cm. in length.

The patient made an excellent recovery.

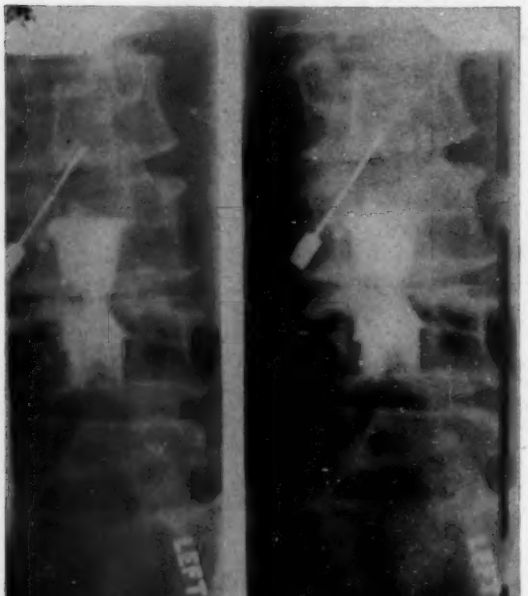

Fig. 2. Case II. Spot roentgenogram with patient in the erect position shows a somewhat oblique line of block at the distal end of the pantopaque column.

Case II. J. B. (Hosp. No. 303464), male, aged fifty-five, complained of low back pain for more than twenty years, which was never severe enough to incapacitate him. His attacks occurred from two to three times a year and were relieved by heat. There was no history of injury. Seven months before admission he developed low back pain radiating down the posterior aspect of his right thigh and leg and aggravated by motion and strain. Four months later the pain radiated down the posterior aspect of his left leg and slight numbness along the inner side of his right foot appeared.

The patient was confortable when examined. Extension of his spine was limited and pain was aggravated by bending sideways and on hyperextension of both legs, more marked on the right side. The right cremasteric and left abdominal reflexes were diminished, and the ankle and knee jerks were absent bilaterally. There were no sensory changes.

Plain roentgenograms of the lumbosacral spine showed narrowing of the lowermost three intervertebral spaces and moderate osteoarthritic changes involving the lower lumbar spine.

Lumbar puncture between the fifth lumbar and first sacral vertebrae was dry. A second tap between the second and third lumbar vertebrae was successful, and manometric determinations at this site were normal. Myelography after the instillation of 3 cc. of pantopaque revealed a complete block at the level of the inferior margin of the fourth lumbar vertebra. The distal end of the column was irregular but not broadened, and a small concave indentation was present. Several radiolucent streaks parallel to the long axis of the cord indicative of swollen nerve roots were present. A shallow indentation in the left side to the pantopaque column at the interspace between the second and third lumbar vertebrae was seen, interpreted as due to a degenerative disc change.

The spinal fluid proteins were 175 mg. per 100 cc., and the globulin content was three plus.

The roentgen diagnosis was obstruction due to central protrusion of a herniated disc. In view of the high proteins the clinical diagnosis favored cauda equina tumor.

A laminectomy of the fourth and fifth lumbar vertebrae was performed. The lesion could not be seen extradurally. When the dura was incised and the cauda equina drawn aside the protruded disc was readily brought into view. The visible protrusion measured 2 by 2 cm. and angulated the cauda equina posteriorly. The disc was removed through a transdural incision, and the patient made an excellent recovery.

Case III. C. K. (Hosp. No. 306573), a male, aged twenty-nine, first complained of low back pain immediately after holding a heavy weight two years ago. He had been flexed for about five minutes and then was unable to straighten his

back. This gradually abated and he was free from pain for about two weeks. The low back pain then recurred and was worse in the morning but improved as the day went on. Periods of remission and exacerbation were frequent, the painful episodes lasting about two weeks. For six months before admission he had more or less constant pain radiating down the posterior and lateral aspects of both thighs and legs as far as the lateral malleoli, and scattered areas of paresthesia were present. The pain was aggravated by straining.

Examination showed a loss of the usual lumbar lordotic curve and pronounced spasm of the erector spinae muscles. There was limitation of flexion and extension with reference of pain to the lateral aspects of both thighs. A bilateral Lasègue's sign was present. The reflexes were normal, and hypesthesia of the right leg up to the thigh was found.

Plain roentgenograms showed straightening of the usual lumbar lordotic curve and narrowing of the lumbosacral interspace.

Myelography after the injection of 3 cc. of pantopaque between the third and fourth lumbar vertebrae showed a complete transverse block at the level of the middle of the fourth lumbar vertebra with dentate serrations in the caudal end of the pantopaque column. Several negative shadows parallel to the long axis of the spinal canal were considered indicative of swollen nerve roots.

About 2 cc. of the pantopaque was removed, and the interspace between the fifth lumbar and first sacral vertebrae was tapped. After the injection of 2 cc. of pantopaque the patient complained of severe pain, no doubt due to distention of the caudal sac. With the patient turned into the head-down position the inferior margin of the blocking lesion was identified at the level of the interspace between the fourth and fifth lumbar vertebrae as a transverse block with two small vertical projections of pantopaque passing between swollen nerve roots. No defects at the lumbosacral interspace were seen. The findings were interpreted as complete block due to a central protrusion of a herniated intervertebral disc. Following examination the

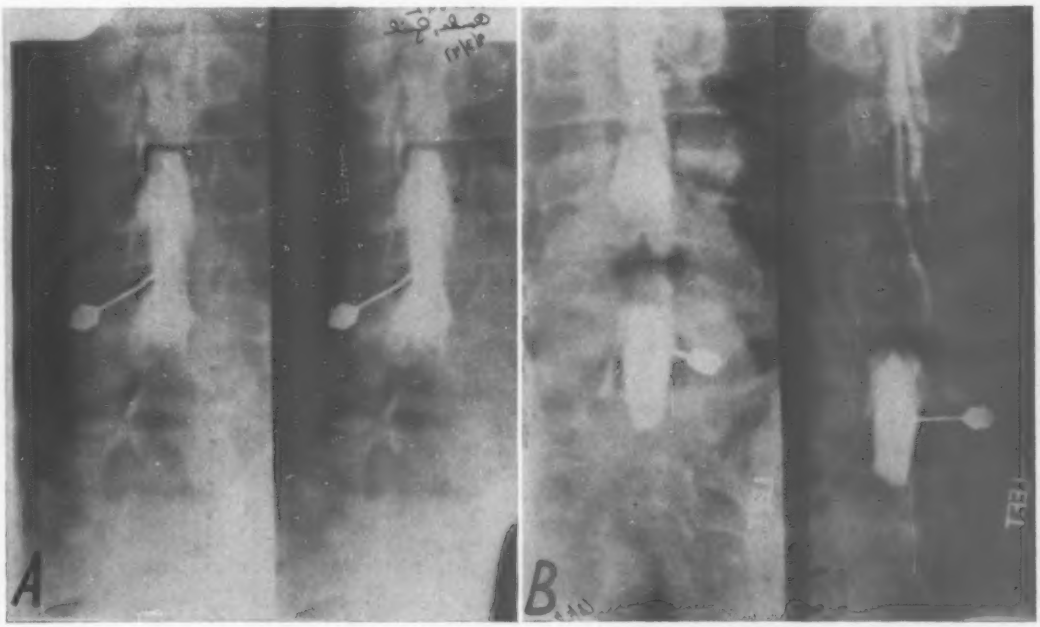

Fig. 3. Case III. *A*, spot roentgenogram with the patient in the erect position shows a transverse block at the midportion of the body of the fourth lumbar vertebra with dentate serrations at the distal end of the column. *B*, the upper aspect of the block is shown with the patient in the erect posture. Two cubic centimeters of pantopaque have been instilled into the caudal sac. *C*, the lower margin of the block is identified with the patient in the head-down position just above the superior margin of the fourth lumbar vertebra.

oil was withdrawn without difficulty and the patient's pain vanished.

Manometric determinations above the level of the block were normal. Below the block manometrics were indicative of a complete obstruction, with an initial pressure of 50 mm. of water, no rise on jugular compression and a rapid fall to zero pressure.

The spinal fluid protein content was 29 mg. per 100 cc. above the block and 31 mg. per 100 cc. below.

Laminectomy of the fourth and fifth lumbar vertebrae was performed. Extradural exploration was negative, but on opening the dura a large midline disc protruding slightly towards the right was readily observed and removed without difficulty through a transdural incision.

The patient made an excellent recovery.

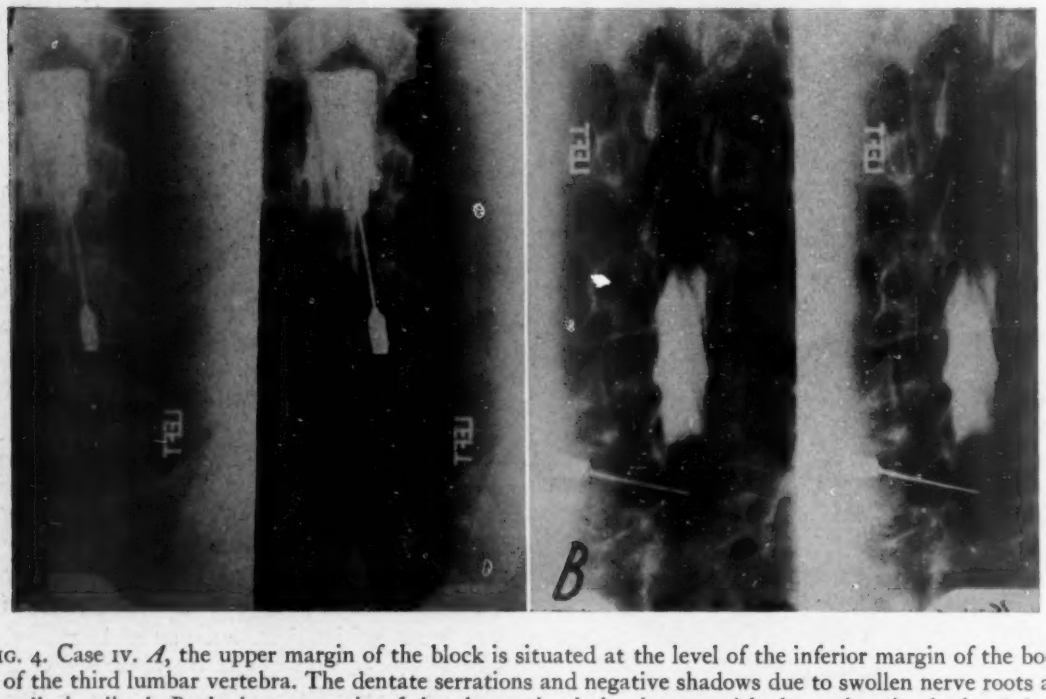

Fig. 4. Case iv. *A*, the upper margin of the block is situated at the level of the inferior margin of the body of the third lumbar vertebra. The dentate serrations and negative shadows due to swollen nerve roots are well visualized. *B*, the lower margin of the obstructive lesion is seen with the patient in the head-down position after the instillation of additional pantopaque into the caudal sac. Swollen nerve roots are seen in this region as well.

Case iv. S. W. (Hosp. No. 305698), male, aged fifty-five, had a sudden knife-like pain in the lower back while lifting a heavy beam three months before admission. He was unable to straighten his back, and the pain was aggravated by slight strain. This disappeared after bed rest, but recurred three weeks later, accompanied by pain down the lateral aspect of the left thigh and leg. He was admitted because of the low back pain.

Examination showed a flattening of the usual lumbar lordotic curve, with limitation of flexion and extension because of pain. There was no tenderness on pressure over the spine or pelvis. Straight leg raising on the right side caused pain on the left side, and raising the left leg produced severe discomfort. No sensory changes or pathologic reflexes were noted. The left knee jerk was slightly reduced.

Plain roentgenographic examination of the lumbosacral spine showed straightening of the usual lumbar lordotic curve and slight arthritic changes in the lowermost two lumbar vertebrae. The intervertebral spaces were normal. A Schmorl's node was seen in the superior surface of the third lumbar vertebra.

Myelography after the injection of 3 cc. of pantopaque revealed a complete obstruction at the level of the inferior margin of the third lumbar vertebra. Several dentate small serrations were seen in the caudal end of the pantopaque column, and linear radiolucent streaks indicative of swollen nerve roots were present.

After removal of the pantopaque, a second spinal needle was inserted into the lumbosacral interspace. Manometric determinations at this site showed a partial block. On tilting the patient into the head-down position the lower margin of the blocking lesion was identified at the level about 1 cm. beneath the inferior margin of the fourth lumbar vertebra. Parallel radiolucent streaks indicative of swollen nerve roots were seen below the level of the block. No defects in the pantopaque column below the block were found. On completion of the examination the pantopaque was removed easily.

The protein content of the cerebrospinal fluid obtained from above the block was 120 mg. per 100 cc.

A laminectomy of the third and fourth lumbar vertebrae was performed. A large herniated disc was found anteriorly and above the interspace between the third and fourth lumbar vertebrae compressing the cord posteriorly. This was removed transdurally and the patient made an uneventful recovery.

Case v. B. F. (Hosp. No. 220577) female, aged thirty-three, had low back pain one year before admission without any known traumatic episode. During the past four months she had had a definite increase in libido. Eight days prior to admission numbness over the lower abdomen, buttocks, perineum and anterolateral aspects of both thighs appeared together with urinary retention requiring catheterization. Obstipation was present for eight days. She also had severe shooting pains down the posterior aspect of both thighs. A sensory level below the first sacral dermatome was elicited bilaterally. The left abdominal reflexes were slightly less active than the right and there was failure of the normal left plantar response. Both ankle jerks were diminished, the left more than the right. About 20 per cent impairment of motor power of the left lower extremity was present.

The clinical diagnosis was cauda equina tumor.

Plain roentgenograms showed no evidence of bony abnormality and the intervertebral spaces were normal.

Myelography after the instillation of 3 cc. of lipiodol between the third and fourth lumbar vertebrae showed a complete obstruction at the level of the superior aspect of the neural arch of the fifth lumbar vertebra. The caudal end of the sac was somewhat oblique, the right side being slightly lower than the left. The defect was rather smooth with a slight convexity in its midportion.

The cerebrospinal fluid proteins were 55 mg. per 100 cc., and the globulin was two plus.

A lumbosacral laminectomy revealed the dura corresponding to the first sacral segment to

Fig. 5. Case v. A somewhat oblique line of block is seen at the level of the neural arch of the fifth lumbar vertebra.

be covered with thickened ligamentum flavum. It was evident that the roots were riding high over an obstruction in the spinal canal. These were pulled aside and a very large protrusion through a much thinned anterior dura indicative of a herniated disc was observed. This was removed transdurally and the patient made an uneventful recovery.

DISCUSSION

A total of 590 cases collected from the

literature examined by means of lumbar myelography, together with the 150 reported here, were reviewed to ascertain the relative incidence of complete spinal canal obstruction with protrusion of the lumbar discs.[1] This did not include series reported in which no cases of complete block were mentioned, a factor which reduces the absolute incidence of this condition. Only those in which the contrast medium was completely unable to traverse the region of block were included. Partial blocks, no matter how pronounced, and transverse defects were not considered within the scope of this presentation. All in all, 27 cases with complete block were found, an incidence of 3.3 per cent.

The longest series of such cases was that of Payne and French, who reported 8 cases out of 90 examined myelographically and verified at operation. The presenting symptoms in this group were chiefly low back pain with subsequent involvement of both legs. There was also weakness of the legs with sensory disturbances there and in the saddle area, urinary and bowel difficulties, muscular atrophy of the glutei, calf and thigh muscles and motor impairment and altered reflexes.

Ver Brugghen[2] reported 9 out of 300 consecutive patients with herniated discs presented symptoms of acute compression of the cauda equina. Myelographic examinations were not made in his series. Clinically the patients presented symptoms of severe sciatica, saddle anesthesia, weakness of the legs and sphincter disturbances. Ankle jerk and knee jerk reflexes were affected in most of his patients. Spinal taps in 3 patients showed complete block.

Hampton and Robinson also reported that complete block due to herniation of the lumbar intervertebral discs may simulate tumors of the cauda equina. Love and Walsh[3] mentioned that block is rare unless paraplegia is present. Arbuckle and Sheldon commented that herniation of the nucleus pulposus and cauda equina tumors may produce similar clinical syndromes which cannot be excluded one from the other on the basis of history and physical findings alone.

In contrast with these reports of severe neurologic disturbances are the first 4 patients in this series. While all had low back pain often aggravated by straining, this was quite variable and periods of remission were frequent. In some there was considerable doubt as to whether a tumor, a disc or for that matter any organic lesion was present. Sensory changes in the saddle area, urinary and bowel difficulties and abnormal plantar reflexes were observed only in the fifth patient diagnosed as having a cauda equina tumor. Absent ankle jerks bilaterally were present in 3, and the knee jerks were diminished bilaterally in one and unilaterally in another patient. Very little motor loss was noted except in the fifth patient. The duration of symptoms varied from three months to over twenty years. Four of the 5 had symptoms for less than two years.

Plain roentgenograms of the lumbosacral spine showed very little change from the normal. Slight arthritic changes were present in 2 patients, quite compatible with their ages. Narrowing of the lumbosacral interspace was present in 2 patients. The intervertebral spaces between the lower three lumbar vertebrae were diminished in 1, and 2 had normal intervertebral spaces. The sites of the herniations did not correspond with the narrowed discs. No changes in the pedicles, laminae or contours of the spinal canal were noted.

The most reliable objective evidence of herniation of the nucleus pulposus is obtained by means of pantopaque myelography. This procedure has a place of special importance in the diagnosis of complete block before the advent of signs of cauda equina compression. The identification of these patients is important, inasmuch as operative intervention removes the possibility of progressive changes. It becomes imperative, then, in selected patients to provide a diagnosis even in the absence of clinical changes of a classical nature. One must not be overenthusiastic

in selecting patients for myelography, but a certain judicial balance is necessary not to exclude certain individuals purely on the basis of underestimating their complaints.

The spinal puncture needle should be inserted between the third and fourth lumbar vertebrae if a low lesion is suspected, and the lumbosacral interspace utilized if there is any reason to suspect a higher site of rupture. In cases with complete block it may become desirable to utilize both sites. Thus, if a complete obstruction is encountered when the pantopaque is injected above the block, further examination is made by instilling an additional 2 cc. of pantopaque below the obstruction after removal of pantopaque from above the lesion. By proper manipulation of the patient on the tilting fluororoentgenographic table the upper and lower limits of the lesion can be identified. This procedure may also be of assistance in eliminating the possibility of double disc extrusions. Two such instances were encountered by Camp and Addington and overlooked because of lack of visualization of the caudal sac. Soule, Gross and Irving also mention this procedure, but do not describe instances of its application.

Before proceeding with myelography a specimen of fluid is withdrawn for total protein determination. Manometric readings made with the needle above the lesion obviously are of little value, and in all the cases reported here were normal. Partial or complete block was found in the 2 patients who had lumbar punctures at the lumbosacral interspace.

The protein content of the spinal fluid in the 5 patients reported here was elevated in 4 and normal in 1 case. The highest protein content was 175 mg. per 100 cc. The lowest, and only one within normal limits, was 29 mg. per 100 cc. French and Payne also observed elevated protein contents, in 1 case over 200 mg. per 100 cc. The importance of this lies in the evaluation of the significance of high proteins. Love[4] has stated that proteins over 100 mg. per 100 cc. are rarely associated with herniated discs, which is not in accord with the above observations.

Myelograms made after the injection of pantopaque above the lesion present a fairly characteristic appearance of the caudal end of the column, which is best seen with the patient in the erect position. In complete block due to extrusion of the nucleus pulposus there is a dentate, somewhat jagged appearance of the caudal end of the column with a transverse or slightly oblique line of block. Streaking of a linear radiolucent character parallel to the long axis of the spinal canal due to swelling of the nerve roots is frequent. This should be distinguished from dilatations of the pial veins which produce a convoluted defect corresponding with the displacement of the contrast medium by tortuous dilated venous channels.[5] The dentate appearance, in my opinion, is due to the compression of the nerve roots by the herniated disc.

The lower margin of the filling defect, as outlined by pantopaque after the instillation of 2 cc. below the lesion, is usually more irregular than the upper aspect and the dentate appearance is less pronounced. Edematous nerve roots may also be seen beneath the block.

Complete spinal canal obstruction frequently occurs with spinal cord tumors. About 20 per cent of these changes occur in the adjacent bony structures[6] and may be demonstrated on plain roentgenograms. Myelographically intramedullary tumors produce a caplike defect with streaks of oil to either side of the spinal canal for a variable distance alongside the tumor, and the axillary pouches along the course of the oil streaks stand out rather prominently.[7] Block due to extramedullary tumors usually reflect the contours of the tumor mass. In the case of perineurial fibroblastomas or neurofibromas this may assume concave filling defects, sometimes multiple and occasionally in the event of multiple tumors overlapping each other. Block due to a meningioma at the interspace between the twelfth thoracic and first lumbar vertebrae was mentioned by Arbuckle and Shelden.

and their illustration was hardly distinguishable from that of a protruded disc. I have observed similar patterns. However, meningiomas low in the lumbar canal are infrequent, and the site of block may prove of value in evaluating the underlying cause. Ependymomas of the cauda equina frequently produce pronounced bony changes with widening of the spinal canal and decalcification of the pedicles and laminae.

Complete block may also be produced by epidural abscess, as noted by Kaplan and Lautkin[8] and Maltby and Pendergrass. Obstruction secondary to metastatic malignancy, lymphomas or leukemia are usually accompanied by bony changes.

Differentiation between a high termination of the caudal sac and complete block at the lumbosacral interspace can be made with the patient erect. High termination of the caudal sac presents a tapered appearance narrowing to a blunt point, readily distinguished from the transverse dentate pattern present with block due to a herniated disc.

At operation it was found that all the discs reported here presented in the midline, similar to the others gathered from the literature. The operative approach, according to our neurosurgical colleagues, is best made transdurally in these cases. It is quite possible for even a large lesion to be overlooked in an extradural exploration, as was the case in 2 of the patients in this series. In these it was only after the dura had been opened and the region of the block thoroughly explored that a relatively small protrusion against the posterior spinal ligament was opened and large discs removed. The obvious inference is that an exploration cannot be considered complete in patients with midline disc herniations unless the dura is opened.

SUMMARY

Five patients with midline extrusion of the nucleus pulposus in the lower lumbar spine with complete spinal canal block are reported. The myelographic appearance associated with this condition when the pantopaque is instilled above the level of the lesion is a more or less transverse block with irregular dentate serrations at the caudal end of the column. When pantopaque is introduced beneath the level of the block the lower margin of the herniated disc is demonstrable as a somewhat more irregular transverse defect and the dentate serrations are less pronounced. This appearance is due to pressure of the herniated disc against the roots of the cauda equina.

Clinically the five patients reported here showed minimal neurologic changes in four and a syndrome diagnosed as cauda equina tumor in the fifth. Other cases gathered from the literature, which presented a similar myelographic pattern with the pantopaque injected above the block, were commonly associated with a more severe neurologic syndrome often indistinguishable from cauda equina compression due to tumor.

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THE ROENTGENOLOGIC DIAGNOSIS OF PROLAPSED GASTRIC MUCOSA*

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PROLAPSE of gastric mucosa into the duodenal bulb was first reported in 1911 by von Schmieden.[33] Since that time less than 50 cases have been reported which were uncomplicated by other coexistent abnormality in the stomach or duodenum; of these, 30 were proved by surgery or autopsy.

The diagnosis of gastric prolapse is a roentgenologic one. Rarely is it suggested by the clinician prior to gastrointestinal examination. We have found it difficult to evaluate the symptomatology since, in our experience, it is frequently discovered coincidentally with other pathological conditions which dominate the clinical picture.

The correct roentgenologic diagnosis of this condition is important since it is frequently mistaken for other more serious diseases.

ETIOLOGY

The etiology of gastric prolapse is as yet undetermined. Rees[27] believes that pyloric narrowing and subsequent hyperperistalsis loosens the mucous membrane and causes it to hypertrophy and prolapse. There was no evidence of pyloric narrowing in our cases. Eliason and Wright[10] propose the theory that a low grade inflammation of the mucosa results in its hypertrophy; contractions of the stomach might then enlarge and lengthen the hypertrophic folds and peristalsis push them through the pylorus. Our pathological studies shed no light on this possible mechanism; 2 of our cases had microscopic examination and both showed evidence of inflammation, but 1 also had a peptic ulcer. Forssell[13] demonstrated that the muscularis mucosae forms a special contractile organ of the mucous membrane and is able to displace the mucous membrane in all directions. Golden[14] described the following changes in the mucous membrane during "antral systole": Normally, by a cephalad movement of the mucous membrane, the mucosal folds change from a transverse direction to a longitudinal one. He believes that if this fails to occur, the transverse folds may be forced into the pylorus during peristalsis. Scott[31] believes that the structural conditions necessary for the development of prolapse are inherent in the walls of the normal stomach, but that prolapse occurs only after the fibers in the flexible submucosa have been stretched and loosened by abnormal gastric peristalsis, which, in turn, is initiated by neurogenic and/or chemical stimuli. He believes that certain neurogenic factors are the exciting causes of a disturbed gastric function which ultimately brings about a mucosal prolapse.

INCIDENCE

Scott[31] saw 14 cases of gastric prolapse in 1,346 upper gastrointestinal series in a one year period at a naval hospital. There were 325 duodenal ulcers, 13 gastric ulcers and no gastric tumors seen during that time. He feels that gastric prolapse occurs more frequently than is generally recog-

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nized, and may be overlooked because the examiner is not thinking of it, confuses it with other pathology, or recognizes but does not report it.

In a twelve month period from August, 1946 to August, 1947, there were 14,809 admissions to the Cincinnati General Hospital, and 10,000 new patients were seen in the out-patient department. The Department of Radiology did 1,257 upper gastrointestinal studies, and 35 cases of gastric prolapse were found. This represents an incidence of 2.8 per cent of all upper gastrointestinal series performed. In the same period 143 duodenal ulcers, 35 gastric ulcers, 30 gastric malignancies and 5 cases of antral gastritis were seen. Duodenal ulcer was approximately four times as common as gastric prolapse; gastric ulcer, malignancy and prolapse occurred with about equal frequency.

Scott's patients were in a younger age group than ours. The incidence of duodenal ulcer in his cases was much higher, but the relative incidence of gastric prolapse and gastric ulcer was approximately the same, just as in our series.

Of our 35 cases, 24 were males and 11 females; 25 were white and 10 colored. The ages of the patients varied between twenty-four and eighty-two, the average age being fifty-two years.

PATHOLOGICAL FINDINGS

Two cases were proved at autopsy and 1 following subtotal gastric resection for prepyloric ulcer. In these 3 cases the gastric mucosa slid easily over the muscularis and could be lifted through the pylorus for distances of as much as 2.5 cm. (Fig. 2).

Scott states that in 126 normal stomachs at postmortem examination it was impossible to pull the gastric mucosa through the pylorus. Bralow and Melamed[6] examined several normal stomachs within three hours postmortem and found that a small amount of gastric mucosa could be pulled through the pylorus, simulating a slight prolapse.

The 3 cases proved by pathological examination are briefly presented:

CASE REPORTS

Case 1. S. F., a colored male, aged sixty-four, was admitted October 3, 1946. A diagnosis of carcinoma of the lung was established. An upper gastrointestinal series revealed only gastric prolapse (Fig. 1). Gastroscopy was performed twice, but the antrum was never visualized. The patient died on November 18, 1946.

The gross pathologic diagnoses were: carcinoma of the lung with widespread metastases;

Fig. 1. Case 1. (S. F.) The base of the duodenal bulb is concave. The deformity is produced by prolapsed gastric mucosa, recognized as negative linear filling defects passing through the pylorus into the bulb. This was confirmed at autopsy.

prolapse of gastric mucosa. The pathological description of the stomach by Dr. Paul Jolly follows: "The stomach is opened along the lesser curvature to a point 4 cm. proximal to the pylorus. With one finger in the duodenum and one finger in the stomach, a flap of gastric mucosa is found in the prepyloric region of the stomach which can easily be pushed back and forth through the pylorus. The stomach and duodenum are then completely opened. The rugae in the distal 15 cm. of the stomach lie in a circular pattern rather than in the usual longitudinal pattern. The mucosa appears quite redundant

and there is a fold of mucosa just proximal to the pylorus which is about 1.5 cm. high. This is easily moved back and forth through the pylorus, the maximum excursion of the free border of this fold being 2.5 cm. (Fig. 2). At a point 5 cm. proximal to the pylorus, the mucosa is easily pulled up into a fold 2.5 cm. high and in so doing the prominent fold at the pylorus is obliterated. The remainder of the gastroenteric tract presents no abnormality either in mucosa, wall or serosa."

Review of the microscopic sections of the stomach by Dr. Edward A. Gall revealed moderate infiltration of the mucosa with plasma cells and lymphocytes.

CASE II. J. B., a white male, aged seventy-four, was admitted to the hospital March 17, 1947, complaining of "swollen stomach," loss of appetite, cramping abdominal pain and diarrhea. A diagnosis of cirrhosis of the liver was made. Barium enema was negative. Examination of the upper gastrointestinal tract revealed esophageal varices and gastric prolapse (Fig. 5, *D*). The patient died on March 29, 1947. The gross pathologic diagnoses were: portal cirrhosis with hemorrhage from ruptured esophageal varices; gastric prolapse. The stomach was dilated with gas and a moderate amount of old bloody fluid. The mucosa was dark red. In the pyloric portion the mucosa was redundant and slid easily through the pylorus into the duodenum for a distance of over 2 cm. There was no gross evidence of inflammatory change. No microscopic sections of the stomach were made.

CASE III. G. C., a colored male, aged fifty-eight, was admitted to the hospital September 10, 1946, with a history of intermittent epigastric pain for several years, occasional hematemesis and tarry stools. Upper gastrointestinal studies revealed a prepyloric ulcer and gastric prolapse (Fig. 3). A gastric resection was advised because of the long history and numerous episodes of bleeding. On September 26, 1946, a subtotal gastrectomy was performed. The resected specimen consisted of a segment of the stomach and duodenum measuring 20 cm. in length. On opening the stomach, two ulcers were found on the distal portion of the posterior wall of the antrum, 2.5 cm. apart, each measuring 0.5 cm. in diameter. The pyloric mucosa was redundant and could be lifted through the pylorus for a distance of 2 cm. Microscopic sections (reviewed by Dr. Edward A. Gall) showed ulceration extending into the muscularis. Surrounding the ulceration there was acute and chronic inflammatory reaction. Sections elsewhere in the stomach revealed chronic inflammation within the mucosa and submucosa. Diagnoses of benign peptic ulcer and subacute and chronic follicular gastritis with erosion were made.

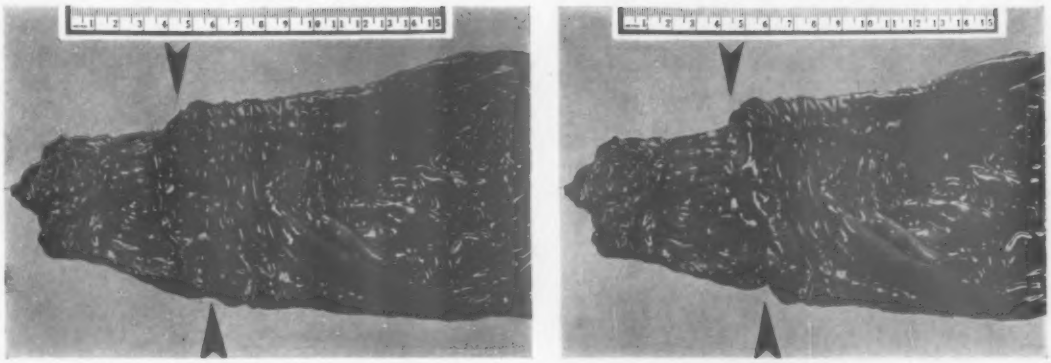
Gastroscopy was performed in 10 of the 36 patients by Drs. Leon Schiff, Carl Kumpe and Stuart Safdi. Prolapse of the gastric mucosa into the pylorus was actually visualized in 2 of the cases. In 7 cases the gastroscopist reported a normal stomach, although in several the antrum was not visualized. One case showed an atrophic gastritis.

SYMPTOMATOLOGY

In an effort to determine whether prolapse produces a characteristic symptom complex, we have divided the 35 cases into two groups: Group 1 (9 cases) had no clinical, laboratory or roentgenologic abnormality except prolapse. Group 2 (26 cases) had abnormal roentgen, clinical or laboratory findings in addition to gastric prolapse.

Brief histories of the 9 cases in Group 1 are presented:

CASE IV. M. C., a white female, aged thirty, was admitted to the hospital October 28, 1946, with a history of constant right upper quadrant pain for one week. There had been some anorexia and nausea, but no vomiting. There had been no hematemesis or melena. Bowel movements were normal. There was no history of food intolerance. Her previous health had always been good. Physical examination revealed only slight right upper quadrant tenderness. Hemoglobin was 12.6 gm. Kahn reaction was negative. A clinical diagnosis of acute hydrops of the gallbladder was made. Oral cholecystogram revealed a normally functioning gallbladder with no evidence of stone. Two barium enemas were negative. An intravenous pyelogram showed normal kidneys. Upper gastrointestinal series revealed gastric prolapse; there was no gastric residue at six hours. She was treated palliatively. The pain gradually subsided and she was discharged, asymptomatic, on November 16, 1946. No definite clinical diagnosis



A *B*

FIG. 2. Case 1. (S. F.) Autopsy specimen of antrum and duodenal bulb. Arrows indicate the proximal end of the pylorus. *A*. The mucosa has been lifted through the pylorus into the duodenal bulb for a distance of 2.5 cm., reproducing the condition recognized roentgenologically during life as gastric prolapse. *B*. The prolapsed gastric mucosa has been reduced.

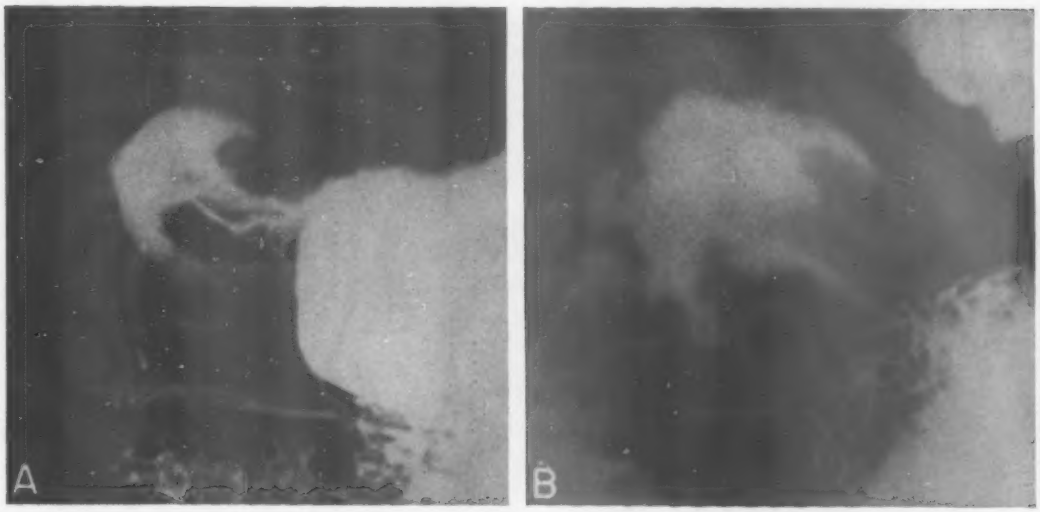


Fig. 3. Case III. (G. C.) "Mushroom" appearance of the bulb due to gastric prolapse. The deformity in *B* might be confused with a polypoid lesion of the bulb. However, in prolapse the appearance of the bulb is constantly changing. Prolapse was confirmed at surgery. The two prepyloric ulcers found at operation are not well shown on these roentgenograms.

was established. She has not returned to the hospital since her discharge.

Case V. W. McK., a colored male, aged fifty-one, entered the clinic in January, 1947, complaining of dyspnea, "sour stomach," heart burn, gas and occasional vomiting for several years. Soda relieved these symptoms. He had been unable to eat fatty foods for years. He had had no episode of hematemesis or tarry stool. Except for moderate consumption of alcohol, the past history was not remarkable. The only positive findings on physical examination were obesity and some elevation of the systolic blood pressure. A clinical diagnosis of peptic ulcer was made. Hemoglobin was 12 gm. Kahn reaction was negative. Electrocardiogram was normal. Cholecystogram demonstrated a normally functioning gallbladder. Roentgenoscopy and roentgenography of the heart revealed cardiac enlargement which was predominantly left ventricular. Upper gastrointestinal studies demonstrated only gastric prolapse; there was no residue in the stomach at six hours. He was and was seen to prolapse into the bulb. The findings were confirmed by gastroscopy.

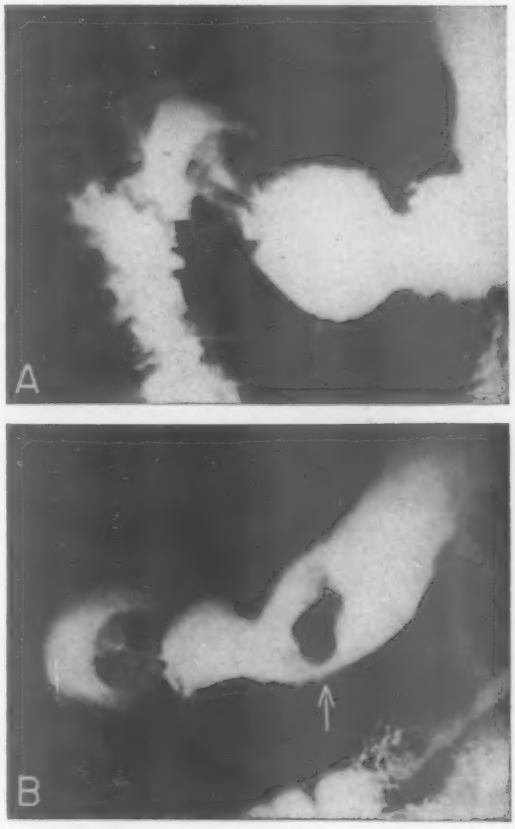


Fig. 4. *A*, Case XIV. (I. L.) Typical "mushroom" appearance of the bulb due to a moderately large gastric prolapse.

B, Case XIII. (L. B.) Marked concavity of the base of the bulb due to a large gastric prolapse. This patient also had a pedunculated gastric polyp (arrow) which moved about freely in the stomach

treated with belladonna, cremalin and a bland diet. At his last visit to the clinic in May, 1947, his symptoms were much improved.

CASE VI. R. B., a white male, aged thirty-eight, was admitted to the hospital on January 31, 1947. One year before, he had experienced an attack of epigastric pain lasting several days and requiring morphine for relief. Following this he was in good health until three months before admission when he had another episode of epigastric pain. The pain again subsided, and he was free of symptoms until eight days prior to admission when the same pain recurred. It was gnawing, intermittent, localized to the epigastrium, and unrelated to food. His physician prescribed cremalin, but this brought no relief. There was some relief with milk. Several days before admission he had had three teeth extracted following which persistent oral bleeding occurred. Several hours before admission he vomited a moderate amount of old blood. Past history revealed the patient to be a heavy drinker, consuming up to a pint of whiskey a day for years. Physical examination revealed only epigastric tenderness and some rigidity. It was not determined whether the vomited blood was coming from a gastric lesion or had been swallowed. A tentative diagnosis of bleeding peptic ulcer was made. Hemoglobin was 16.0

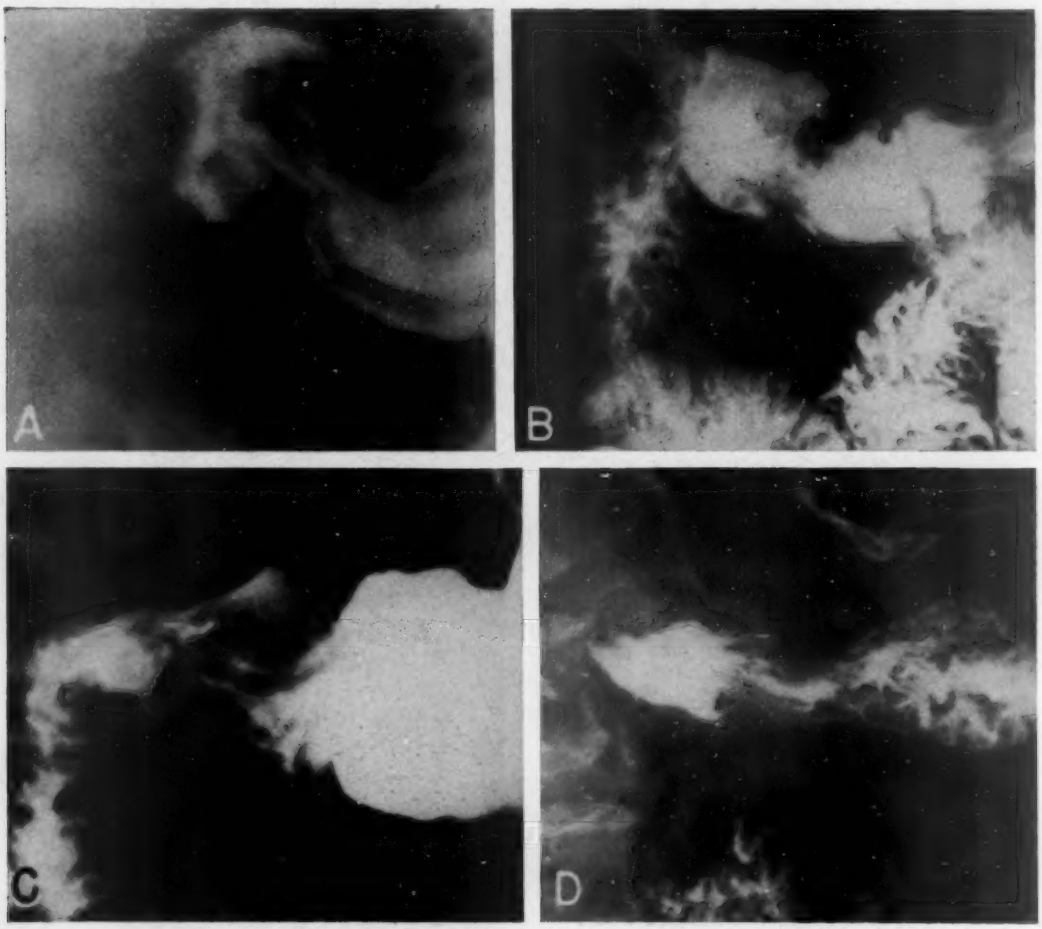


FIG. 5. *A* and *B*, Case XV. (W. A.); *C*, Case XVI. (M. G.), and *D*, Case II. (J. B.) Three cases demonstrating gastric mucosal folds passing into the duodenum. The folds are visualized as negative linear filling defects between the thin lines of barium. In the case illustrated in *D* (Case II) prolapse was confirmed at autopsy; the redundant gastric mucosa in the antrum was easily lifted through the pylorus for a distance of approximately 2 cm.

gm. Kahn reaction was negative. Electrocardiogram was normal. Two upper gastrointestinal studies were done. Both revealed gastric prolapse (Fig. 7) with no gastric retention at six hours. The patient was put on a Sippy diet, antacids and antispasmodics. His improvement was rapid and he was discharged, asymptomatic, on February 7, 1947. He has not returned.

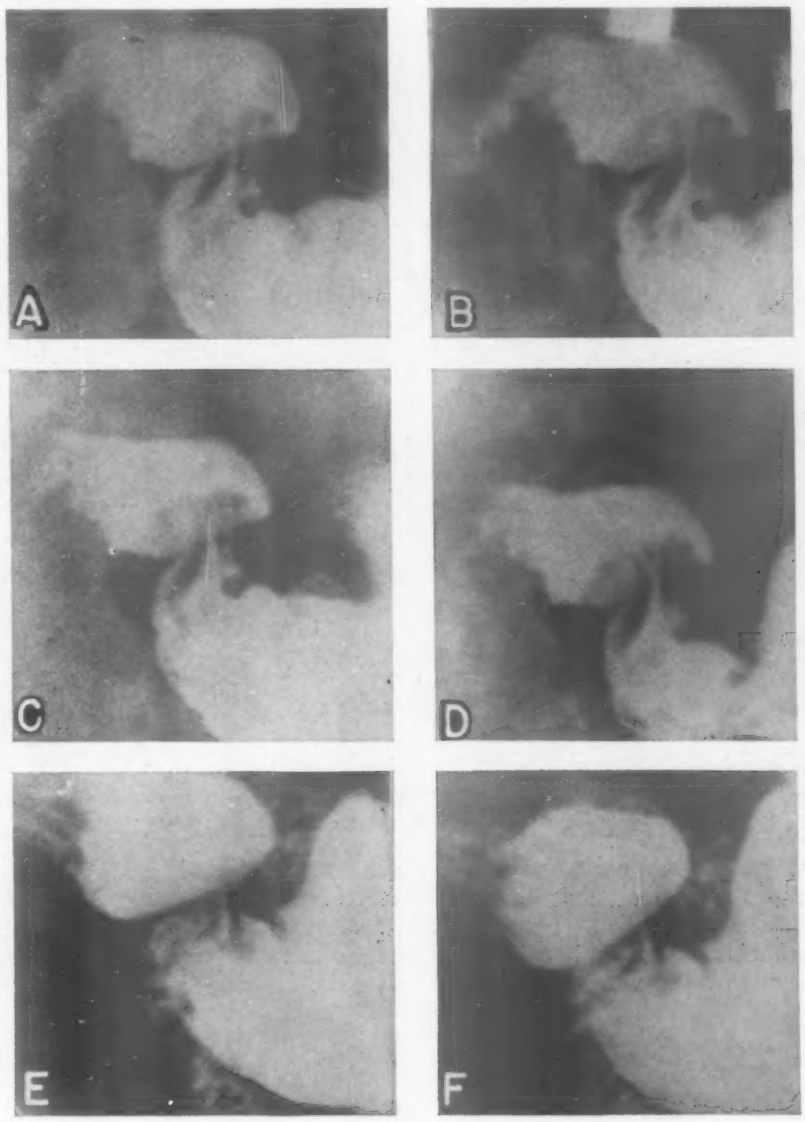


Fig. 6. Case xvii. (H. McK.) Roentgenograms taken in rapid succession with multigraph spot device. *A*, *B*, *C* and *D*, concavity of the base of the bulb due to prolapse. Gastric mucosal folds can be traced through the pylorus. *E* and *F*, prolapse is reduced. Bulb now appears normal.

Case vii. A. F., a colored female, aged forty-three, came to the clinic in February, 1947, complaining of nausea, vomiting, and intermittent attacks of sharp epigastric pain for the past ten years. She denied hematemesis or melena. In 1938 she was discovered to have late syphilis following which she received adequate treatment. In 1946 the patient was admitted following an acute attack of severe upper ab-

dominal pain and vomiting. At that time she was thought to have mechanical small bowel obstruction. She was treated expectantly, the symptoms rapidly disappeared, and she was discharged with no definite diagnosis four days after admission. She had had no complaints for the past several months until the onset of the present illness. Physical examination was essentially negative except for obesity. The clinical diagnosis was probable peptic ulcer. Hemoglobin was 15 gm. Kahn reaction was negative. Oral cholecystogram revealed a normally functioning gallbladder. Barium enema study was negative. Upper gastrointestinal series demonstrated gastric prolapse; no barium remained in the stomach at six hours. The patient was treated with antacids and started on a reduction diet. Her symptoms improved rapidly and when last seen in the clinic in March, 1947, she was asymptomatic.

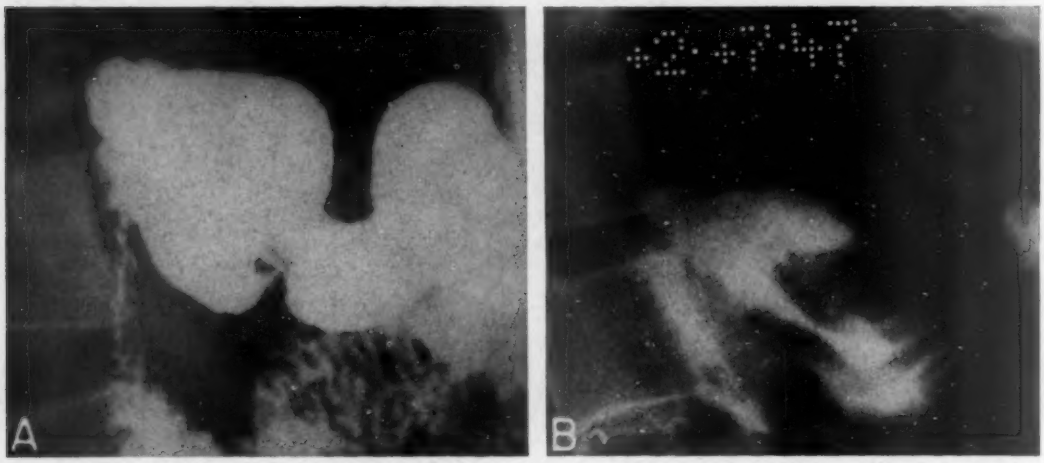


FIG. 7. Case VI. (R. B.) *A*. There is slight concavity of the base of the bulb. Gastric rugae passing through the pylorus are partially obscured by barium. *B*. Roentgenogram taken several minutes later. Appearance of the bulb has changed. There is greater concavity of the base.

CASE VIII. G. D., a white male, aged forty-one, visited the clinic in March, 1947, with a history of recurrent episodes of epigastric pain for one year. They occurred when the stomach was empty and were relieved by food, milk and antacids. The pain never awakened the patient at night. He experienced occasional nausea and vomiting but no hematemesis or tarry stools. Fried foods precipitated his symptoms. The patient was a known chronic alcoholic. Physical examination was normal except for slight epigastric tenderness. The clinical diagnosis was probable peptic ulcer and chronic alcoholism. Hemoglobin was 15.5 gm. Three upper gastrointestinal series were done at monthly intervals and gastric prolapse was found (Fig. 8, *E* and *F*). On no examination was there a six hour gastric residue. The clinician stated that he believed this patient's symptoms were due to gastric prolapse. He was treated with a Meulengracht diet, belladonna and cremalin. His symptoms improved and when last seen in the clinic in June, 1947, he had no complaints.

CASE IX. R. H., a white male, aged forty, came to the clinic in March, 1947, with a history of nausea, vomiting and recurrent attacks of mild epigastric pain for several years. The pain was in part relieved after ingestion of food or soda. He denied hematemesis and melena. Physical examination was entirely negative. A diagnosis of probable peptic ulcer was made. Upper gastrointestinal series revealed gastric prolapse; no barium was seen in the stomach at six hours. He was put on a regimen of bland diet and amphogel. He was last seen in the clinic in April, 1947, at which time his symptoms had improved.

CASE X. F. P., a white male, aged forty-three, was first seen in April, 1947, complaining of intermittent attacks of epigastric distress, nausea and vomiting for several years. The distress was worse at night when his stomach was empty. It was relieved by food, milk and soda. He had

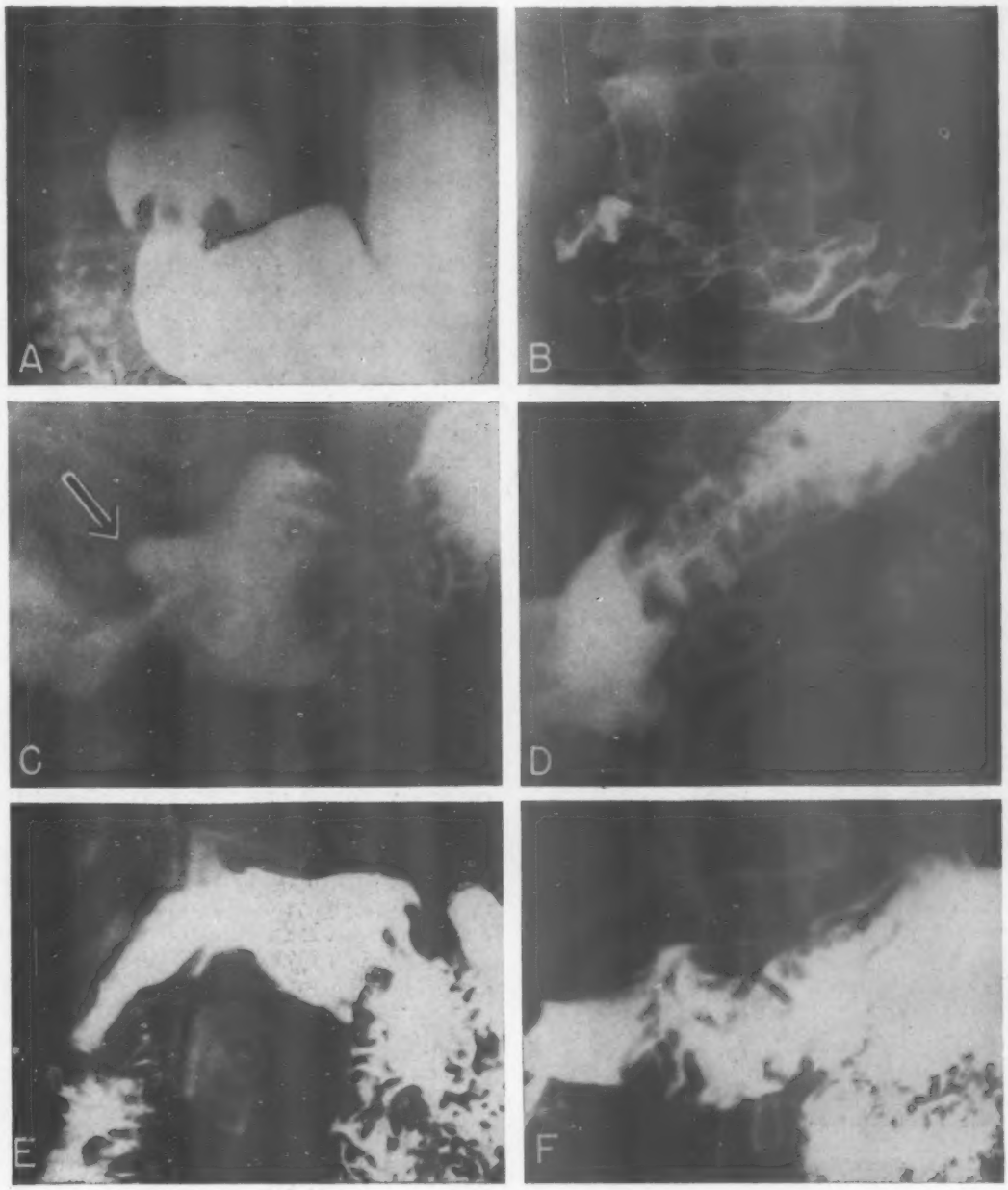


Fig. 8. *A* and *B*, Case xviii. (I. T.) In *A*, gastric mucosa is prolapsed into the bulb producing a "mushroom" appearance. *B* demonstrates the reduced phase. Redundant mucosal folds are piled up in a transverse direction in the antrum. *C* and *D*, Case xix. (R. T.) In *C*, gastric folds are passing through the pylorus and into the duodenum. There is slight concavity of the base of the bulb. An ulcer niche (arrow) is demonstrated at the apex of the bulb. In *D* the prolapse is almost completely reduced, and redundant gastric mucosa has assumed a transverse position in the antrum. *E* and *F*, Case viii. (G. D.) In *E*, there is slight concavity of the bulb due to prolapse. In *F*, the prolapse is reduced; gastric mucosa is piled up in transverse folds in the distal portion of the stomach.

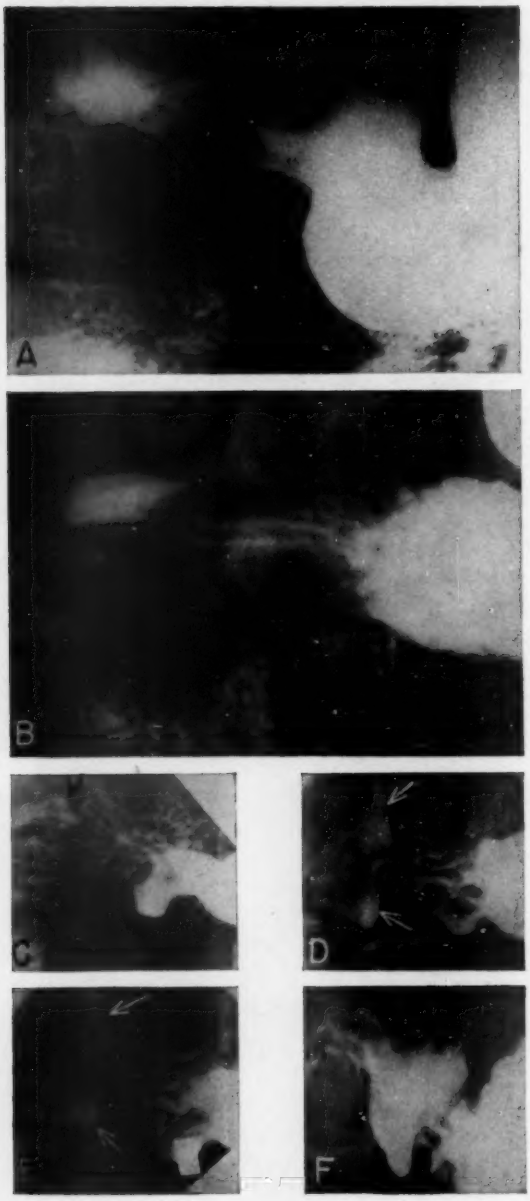


FIG. 9. *A* and *B*, Case IV (M. D.) In *A*, gastric mucosa passes into the duodenum producing slight concavity of the bulb. In *B* prolapse is reduced; gastric folds assume a horizontal position. *C*, *D*, *E* and *F*, Case XX (C. R.) Roentgenograms taken in rapid succession with the multigraph spot device. Arrows indicate base of bulb. In *C*, gastric rugae pass into the duodenum causing concavity of the base of the bulb. In *D*, the prolapse is reduced; gastric folds lie in a horizontal position in the antrum. In *E* and *F*, there is beginning invagination of gastric mucosa with some concavity of the base of the bulb.

never had hematemesis or tarry stools. Physical examination was normal. A diagnosis of peptic ulcer was made. On examination of the upper gastrointestinal tract, gastric prolapse was demonstrated. There was no gastric retention at six hours. The patient was treated with belladonna and a bland diet and was asymptomatic within one month. When last seen at the hospital in July, 1947, he had no complaints.

CASE XI. J. F., a colored male, aged forty, visited the clinic in May, 1947, with a history of intermittent pain in the upper abdomen, worse at night, for the past year. He had had much belching but no nausea, vomiting or tarry stools. Past history was non-contributory. Physical examination was not remarkable. A clinical diagnosis of peptic ulcer was made. Hemoglobin was 15 gm. Kahn reaction was 4 plus. Upper gastrointestinal studies revealed gastric prolapse. There was no gastric residue at six hours. The patient was treated with antacids and antispasmodics and was given antiluetic therapy. At his last visit to the clinic in July, 1947, he had been symptom free for three weeks.

CASE XII. E. S., a white male, aged twenty-nine, came to the clinic in June, 1947, complaining of epigastric discomfort, nausea and occasional vomiting for ten years. He obtained relief from these symptoms with food and soda. There was no history of hematemesis or melena. He was a known chronic alcoholic. Two years ago his family physician told him that he had a duodenal ulcer. He was followed in the psychiatric clinic in 1946 with a diagnosis of anxiety neurosis with paranoid trends. Except for slight epigastric tenderness, the physical examination was not remarkable. The clinical diagnosis was peptic ulcer. Hemoglobin was 14.5 gm. An upper gastrointestinal series revealed only gastric prolapse; no gastric residue was seen in the stomach at six hours. The patient was treated with belladonna, cremalin and Meulengracht diet. He was last seen in the clinic in the latter part of July, 1947, and felt much improved.

These 9 patients present quite similar clinical pictures. The commonest complaint was recurrent attacks of epigastric pain or distress, often relieved by food, milk or alkalies. This occurred in 8 of the 9 patients. Nausea, vomiting, gas and belching were frequent symptoms. Two patients com-

plained of intolerance to fried or fatty foods. In most cases the symptoms began at least one year prior to roentgen examination.

In only 1 patient was there hematemesis (Case VI). However, this patient had had dental extractions just prior to admission and it was believed that the hematemesis probably resulted from swallowed blood.

In no case was an abnormally low hemoglobin found. Hematemesis, melena and secondary anemia in association with prolapse have been reported frequently in the literature.[3,5,9,21] They were not present in the uncomplicated cases in our series.

Four of the 9 patients in Group 1 were consumers of alcohol, and 3 of these were classified as "heavy drinkers."

Four patients had some degree of epigastric tenderness.

The diagnosis prior to roentgen study in 8 of the 9 patients was peptic ulcer; in the ninth, hydrops of the gallbladder was suspected.

The similarity of the symptoms in these 9 patients, and the absence of any other findings which might explain them, leads one to suspect that they might have been produced by gastric prolapse. A number of cases reported in the literature presented clinical histories not unlike those in our 9 patients. However, the evidence is still inconclusive, and for the present we cannot be certain that gastric prolapse is a clinical entity.

Treatment of the patients in Group 1 was medical; bland diet, antacids and antispasmodics were prescribed. In every case there was improvement. Several patients were asymptomatic within one month. However, follow-up has been for a relatively short period of time. There is no apparent explanation for the symptomatic relief from these measures. Scott also advocates sedation and states that freedom from tension, strain, fear and worry (factors which might produce disturbed gastric function) brings improvement. The literature refers frequently to the surgical treatment of prolapse.[2,19,22,24,25,26] McKenzie believes the indications for surgery are threefold: (1) equivocal roentgen signs of prolapse from which a lesion necessitating operation (e.g. a neoplasm) cannot be definitely differentiated; (2) continued bleeding; (3) evidence of pyloric obstruction. In none of our cases was surgery deemed necessary.

Table 1 lists the coexistent conditions found in the 26 cases in Group 2. In several patients more than one other abnormality was discovered. Because the other processes frequently dominated the clinical picture, no effort has been made to evaluate what part prolapse might have played in production of symptoms or signs in these cases.

TABLE I

COEXISTENT CONDITIONS FOUND WITH GASTRIC PROLAPSE IN 26 PATIENTS

Condition	No. of Cases
Diverticula of colon	5
Duodenal ulcer	3
Cirrhosis of liver	3
Heart disease	3
Non-functioning gallbladder	2
Gastric ulcer	2
Probable gastric polyp	2
Carcinoma of lung	2
Carcinoma of ovary	1
Carcinoma of colon	1
Carcinoma of pancreas	1
Foreign body in colon	1
Esophageal varices	1
Polyp of colon	1
Antral gastritis	1
Pedunculated, prolapsing gastric polyp (confirmed by gastroscopy)	1

ROENTGEN FINDINGS

The roentgen findings in gastric prolapse are as follows:

1. There is inconstant deformity of the duodenal bulb. The bulb assumes a "mushroom" appearance, with concavity of the base, when gastric mucosa is invaginated into it (Fig. 4).

2. Mucosal folds are seen passing from the stomach into the duodenum (Fig. 5).

They are visualized as multiple negative linear filling defects. A single rugal fold may normally pass through the pylorus, and this must not be mistaken for prolapse.

3. The appearance of the bulb varies as the gastric mucosa slides back and forth through the pylorus (Fig. 6 and 7).

4. When the prolapse is temporarily reduced, redundant mucosa may pile up in the antrum assuming a circular or transverse direction rather than the usual longitudinal one (Fig. 8); or, it may assume a horizontal direction and appear normal (Fig. 9). During the reduced state there is no deformity of the bulb.

5. Peristaltic waves pass through to the pylorus normally.

6. There is usually no narrowing or elongation of the pyloric channel.

7. The size of the folds is normal.

8. No ulcer niche is demonstrable in the pylorus or duodenum.

9. There is no irritability of the duodenal bulb.

10. Although there is frequent reference to gastric retention in the literature[4,9,26] in none of our cases in Group 1 was this seen.

The importance of prolapse lies in its differentiation from other more serious pathology. In one of our cases the roentgen findings were at first erroneously interpreted as duodenal ulcer. On re-examination, prolapse was recognized as the cause of deformity of the bulb.

DIFFERENTIAL DIAGNOSIS

1. Carcinoma of the antrum: There is a constant deformity of the antrum, and the rugal pattern is usually destroyed. Peristalsis is altered or absent in the involved area. Rarely is the duodenal bulb affected. A mass may be palpable.

2. Duodenal and pyloric ulcer: The ulcer niche is often demonstrable. In duodenal ulcer there may be irritability and spasm of the bulb with resultant constant deformity; the prepyloric folds are normal. In pyloric ulcer the mucosal folds about the involved area may be distorted and peristalsis may not pass through them. No gastric rugae can be demonstrated passing through the pylorus. There is often a six hour gastric residue as a result of pyloric obstruction.

3. Hypertrophic pyloric stenosis in adults:[1,8,18] This condition is characterized by an elongated, narrowed pyloric channel, often with an excentric axis. Occasionally a narrow crevice or rounded depression is demonstrated at the midpoint of the lower border of the canal, resembling a niche. There is concavity of the base of the bulb (similar to that seen in prolapse) which, according to Kirklin and Harris,[18] is due to partial invagination of hypertrophied muscle into the duodenum and is an important diagnostic criterion of this condition. However, the defect is constant, and rugae cannot be traced into the base of the bulb.

4. Antral gastritis: The rugae in the distal portion of the stomach are swollen, thickened and coarse.[11] Cole[7] describes their appearance as similar to "night crawlers." They may produce a constant filling defect in the antrum through which peristalsis may or may not pass.[32] The pyloric channel may be narrowed. However, the bulb is normal, facilitating differentiation from gastric prolapse.

5. Duodenal polyp or papilloma:[30,34] This rare condition[15,16,23] produces a constant vacuolated or multilocular smooth filling defect in the bulb. The pylorus appears normal and gastric rugae cannot be traced through it.

6. Benign gastric tumors: These are rare.[12,25,28] They may be visualized as radiolucent filling defects surrounded by intact mucosa through which peristalsis passes normally. Rugae in the antrum appear normal and there is no deformity of the bulb. In such instances differentiation from prolapse is not difficult. However, gastric tumors may be pedunculated and prolapse into the bulb,[20] or they may slide through the pylorus on prolapsing gastric mucosa. Differentiation in such cases is difficult.[9] Rubin[29] describes a case diagnosed preoperatively as prolapsed gastric mucosa, but at surgery prolapsing gastric polyposis

with carcinomatous degeneration was found. Appleby[2] cites a similar case. There is frequently obstruction in these cases and six hour gastric residue is common.

One confirmed case of prolapsing gastric polyp was seen in the Department of Radiology during the one year period of this study.

Case xiii. L. B., a white male, aged eighty, was admitted to the surgical service with an infected abrasion of the right hand on February 10, 1947. He had multiple vague complaints. Physical examination was essentially negative. Kahn reaction was 3 plus. Two upper gastrointestinal roentgen series in March, 1947, revealed a gastric polyp measuring approximately 2.5 cm. in diameter arising just above the incisura of the stomach and apparently hanging from a pedicle. It moved freely about within the stomach and was seen to prolapse into the duodenal bulb several times. A large prolapse of gastric mucosa into the bulb was also demonstrated. On gastroscopy the polypoid lesion was seen projecting into the lumen of the stomach in the region of the antrum. It was constantly moving and on two occasions it swept through the pylorus accompanied by the redundant gastric mucosa. Due to the patient's age, operation was not advised. He was discharged on March 20, 1947, and has been followed in the clinic. At his last visit in July, 1947, he had no complaints referable to the gastrointestinal tract.

7. Duodenitis: This should offer no differential problem. Kirklin[17] describes the bulb as small, irritable and spastic, with coarse reticular mucosal pattern. There is irritability and distortion of the mucosa of the duodenum distal to the bulb occurs.

SUMMARY AND CONCLUSIONS

Prolapse of the gastric mucosa is not uncommon; thirty-five cases were seen in the Department of Radiology of the Cincinnati General Hospital in a twelve month period. The incidence was approximately the same as that of gastric ulcer. It was frequently discovered coexisting with other intra-abdominal pathology. In one-fourth of our cases in which no other abnormality was found, symptoms suggested peptic ulcer, and that diagnosis was made clinically in eight of the nine patients prior to gastrointestinal roentgen studies. That these symptoms were related to gastric prolapse is suspected, but this relationship has not been convincingly established. The roentgen findings in prolapse are diagnostic but must be differentiated from other more serious conditions. In our nine uncomplicated cases, medical treatment brought rapid improvement in symptoms.

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ARACHNODACTYLY (MARFAN'S SYNDROME)*

TWO CASE REPORTS WITH ETIOLOGICAL IMPLICATIONS

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RECENTLY Tobin and his associates[11] reported clinical data and complete data on the necropsies of 2 adults with arachnodactyly both of whom died as the result of a dissecting aneurysm of the aorta. In their report they reviewed the literature on this syndrome, stating that "Although over 200 cases of arachnodactyly have been reported, descriptions of only twelve autopsied are found in the literature, of these ten are more or less complete descriptions." They stated that the role of the endocrine glands, particularly the hypophysis, remains obscure.

It is the purpose of this paper to present 2 cases of arachnodactyly, one with dislocated lens, tremulous iris and an enlarged sella turcica; the second case had a small sella turcica and no dislocation of the lens. An explanation of the findings will be given.

In 12 autopsied cases of arachnodactyly as reported by Tobin and associates 10 had cardiac disturbances. Four had an increase in the eosinophil cells of the pituitary and the 2 reported by the Tobin group also had this same finding, making a total of 6 of the 14 autopsied cases. Of this total 4 pituitaries were reported as normal; one had a cyst of the gland and 3 had no report on the pituitary. Thus pathological lesions of the pituitary are a common finding.

Tobin stated that their 2 cases had a high arched palate the significance of which will be discussed later. They also stated that the jaw juts forward but the opposite is true in my 2 cases (Fig. 2 and 9).

CASE 1. The patient was a white six year old male of Italian parentage who was brought to the referring ophthalmologist, Dr. Ralph Pino, because of visual disturbance and failure of body development. He weighed 8 pounds and 7 ounces at birth (3.8 kg.). He talked at ten months, walked at fifteen months, and teeth first appeared at the age of three months. It was noted that his hands and feet were longer than normal. He had received roentgen therapy for an enlarged thymus at the age of two years. It was also noted at about the age of fifteen months that his back was not straight. Soon after birth it was noted that he perspired a great

FIG. 1. Case 1. Front view showing the physical characteristics of arachnodactyly.

* From the Department of Medicine and Clinical Research, Harper Hospital.

deal. As he grew older the long spindly type of extremities developed; likewise the head assumed a dolicocephalic shape also characteristic of arachnodactyly.

Past History. At the age of two and a half years his tonsils were removed. He gave a history of measles, "strep throat" and "intestinal flu." He had been seen by two orthopedic surgeons because of the skeletal deformities. He was precocious in his learning. No rheumatic history was present.

FIG. 2. Case 1. Lateral view. The dolichocephalic head, winged scapulae, subluxated ankle joints are shown.

Family History. The father was living, his height was 68 inches (172.7 cm.) and he weighed 150 lb. (68.0 kg.). The mother was living; she was short and undernourished, the height being 61 inches (154.9 cm.) and she weighed 98 lb. (44.5 kg.). There was no familial history of arachnodactyly. The maternal grandmother had diabetes mellitus. A paternal cousin had epilepsy and another paternal cousin had strabismus. Of importance is the fact that both parents had a high arched palate as did the patient. There was no consanguinity in the parents.

Physical Examination. The patient was a slender boy with a marked dolicocephalic head (Fig. 1 and 2). The body measurements were as follows (normal measurements are given for comparison):

	PATIENT		NORMAL	
	inches	cm.	inches	cm.
Head	20.5	(50.8)	20.5	(50.8)
Chest	21.0	(53.34)	22.7	(55.88)
Waist	19.5	(48.26)	20.9	(53.34)
Span	47.0	(119.38)	44.0	(111.76)
Upper	24.0	(60.96)	24.0	(60.96)
Lower	22.5	(56.0)	21.0	(53.34)
Height	46.5	(116.96)	45.0	(114.30)
Weight	36 lb.	(16.3 kg.)	43.9 lb.	(20 kg.)

The referring ophthalmologist, Dr. Ralph Pino, reported as follows:

"From the eye standpoint this child has a dislocated lens that appears from a tremulous iris. We were not able to dilate the pupils sufficiently to make an intraocular examination that is satisfactory. It would appear that the luxation of the lens is not sufficiently marked to interfere too much with vision in this stage. As the child grows older I would anticipate there would be greater luxation." The external occipital protuberance and the supraorbital ridges were prominent. The eyes were prominent. The pupils were small. The ears were prominent and the lower lobes flared outward. The teeth were in only fair condition, several showed caries. Malocclusion with recession of the lower jaw was present. There was a high arched palate. The thyroid gland was palpable. The chest was deformed and the scapulae were of the winged type due to the poor musculature development. The spine showed scoliosis in the thoracic region. The heart was ptotic and there was a loud systolic murmur heard all over the precordium; this had its loudest intensity at the base of the heart. The pulmonic second sound was accentuated. The blood pressure was systolic 112, diastolic 66. The pulse rate was 74 and regular. The liver was not palpable. The genitalia were fairly well developed and both testicles were in the scrotum. The joints of the elbows, knees and ankles were enlarged. There was hyperextensibility of the elbows and knees. The extremities

were long and spindly in character. There was subluxation of the ankle joints. The fingers and toes were abnormally long. The musculature was poorly developed and hypotonic. There was a generalized absence of subcutaneous fat. The capillaries of the extremities were dilated and this gave them a bluish tinge. Some hirsutism of the arms and legs was present.

The urinalysis was normal. The hemoglobin was 80 per cent (12.5 gm.). There were 3,200,000 erythrocytes, 7,200 leukocytes with a normal differential count.

Roentgenograms were reported as follows:

Skull: The tables of the skull are relatively thin with a minimal amount of diploic structure. The anteroposterior diameter of the skull

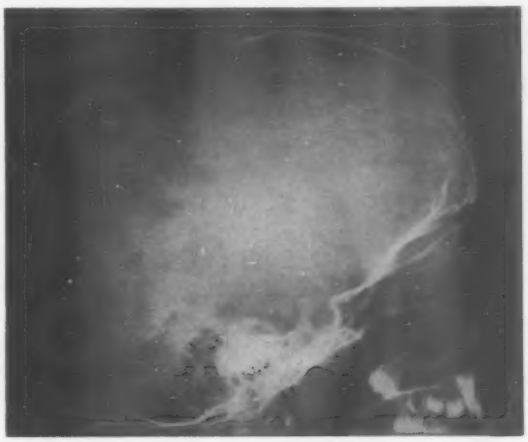

Fig. 3. Case 1. Roentgenogram of skull showing enlarged sella turcica.

is slightly greater than the average and the transverse diameter of the skull somewhat reduced as compared with the average. This gives a configuration somewhat suggestive of the dolicocephalic type of skull. The pituitary fossa is unusually deep. The convolutional markings on the inner table are slightly prominent. There is no unusual intracranial calcification and the mastoid and paranasal sinus development is relatively normal (Fig. 3).

Spine: Examination of the spine in both anteroposterior and lateral projections demonstrates a mild degree of scoliosis with the convexity of the curve to the right in the dorsal level. All of the bone structure is lacking slightly in mineral salt content. There is a spina bifida of the first and second segments of the sacrum (Fig. 4).

Fig. 4. Case 1. Roentgenogram of spine showing scoliosis.

Pelvis: No definite abnormality of the pelvis except for a minimal lack of mineral salt con-

Fig. 5. Case 1. Roentgenogram of pelvis. The exostosis or osteochondroma is seen in the right femur.

FIG. 6. Case I. Roentgenogram of the right hand. There is demineralization of all the bones with elongation of the metacarpal bones and the phalanges of the digits.

tent of the bone structure. There is a suggestive osteochondroma on the inferior aspect of the lesser trochanter of the right femur (Fig. 5).

Hand: Film of the hand in the dorsopalmar projection demonstrates normal ossification of the bone structure, though all the bones are lacking in calcium content, and there is some elongation of the metacarpal bones and the phalanges of the digits. The entire configuration is that of arachnodactyly (Fig. 6).

Conclusions: All of the bone changes in skull, spine, pelvis and hand are rather characteristic of those seen in the so-called Marfan's syndrome, in which there is an associated arachnodactyly.

The keto-steroid output was 2.9 mg. in twenty-four hours which was high since a normal for this age is 1 mg.

The follicle stimulating hormone excretion for a twenty-four hour period was less than 7 mouse units which is normal for this age.

These studies were made, however, after the patient had been on methyl testosterone for approximately two months but none had been given a month previous to the keto-steroid and gonadotropin studies. (Contrast this with second case.) He was placed on 20 mg. of methyl testosterone on September 26 and by October 20 he had gained 3½ lb. On November 1 he developed an acute cold and due to the fever and anorexia he lost 1½ lb. However, by December 6, he weighed 40 lb. (18.1 kg.).

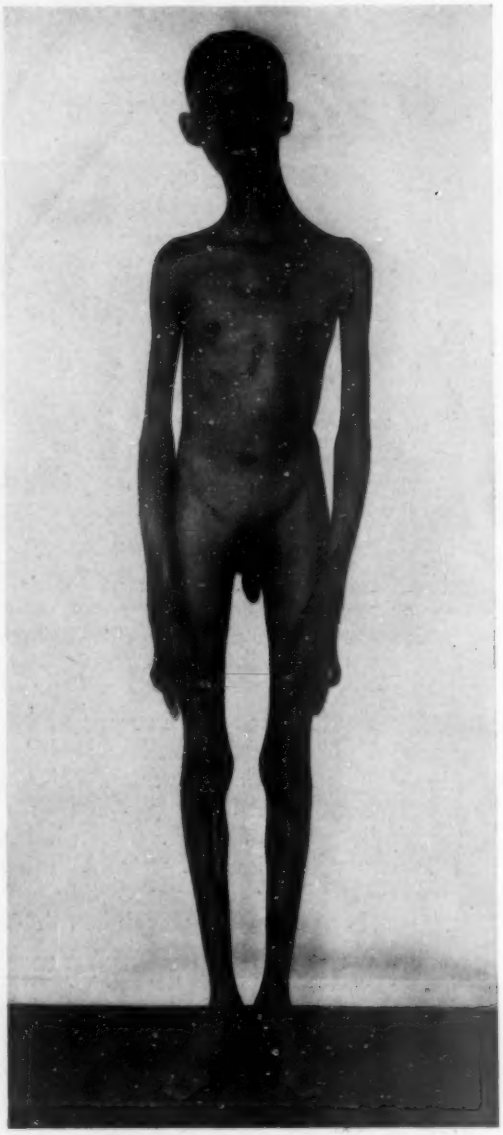

FIG. 7. Case II. Front view. The long arms are well shown, as is the asymmetry of neck, asthenic habitus.

Of importance are the changes noted in the span and height on this form of therapy: the span increased from 47 inches (119.3 cm.) on September 26, 1947 to 49 inches (124.46 cm.) on December 6, 1947, a gain of 2 inches (5 cm.). The height during this period of approximately two months increased from 46.5 inches (117 cm.) to 47.25 inches (119.8 cm.), a gain of $\frac{3}{4}$ inch (1.8 cm.).

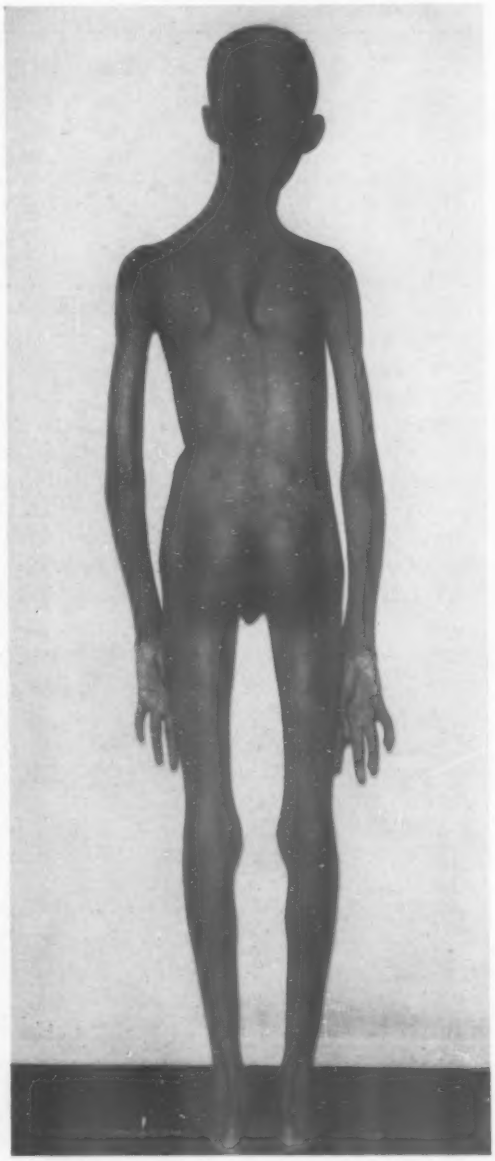

Fig. 8. Case II. Posterior view showing winged scapulae, spindly arms and legs.

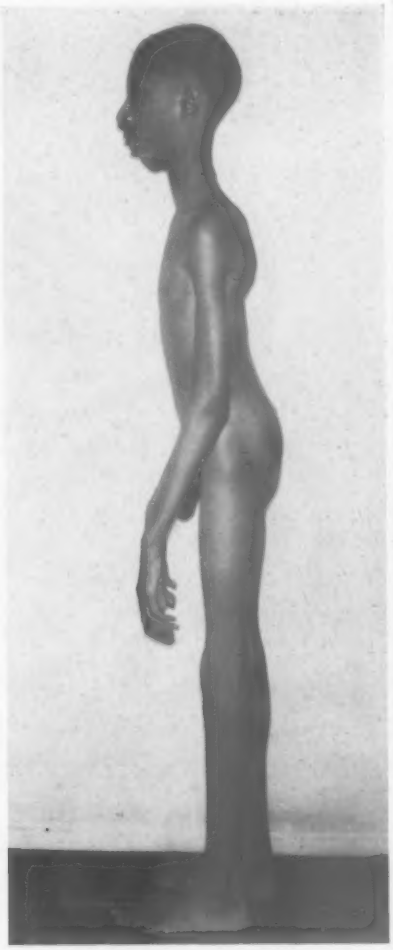

Fig. 9. Case II. Lateral view showing the general body build, and in an exaggerated degree the long spindly arms and legs. The recession of the lower jaw is well shown.

Case II. The patient was a fourteen year old colored boy. The history was not reliable since contact was through an "uncle." He had always been too thin and was always weak. He had previously been examined at Receiving Hospital and it was through the courtesy of the hospital staff and Mr. Arthur E. Parks,* a junior medical student, that this case is reported. Mr. Parks did the keto-steroid and gonadotropin studies on both cases. The "uncle" stated that the patient never looked "natural." Dizziness was complained of by the patient.

The physical examination showed a boy of

* From the Endocrine Laboratory of the Department of Research, Harper Hospital.

FIG. 10. Case II. The high arched palate which is characteristic of cases of arachnodactyly.

asthenic build, undernourished, with the appearance of arachnodactyly (Fig. 7, 8 and 9). The skull was of the dolicocephalic type, the supraorbital ridges were prominent. There was no dislocation of the lens. The pupils were small but reacted normally. The auricles of the ears were large and protruding. The teeth were in fair condition with malocclusion and a recession of the lower jaw. The palate was of the high arched Gothic type (Fig. 10). The thyroid gland was small. The chest was deformed due to scoliosis. The scapulae were of the winged type. The scoliosis produced a marked asymmetry of the neck, chest and lumbar muscles. The heart was ptotic and a loud systolic murmur was heard all over the precordium with the loudest intensity over the aortic area. It was believed that a congenital cardiac anomaly was present but the type was not further determined. The pulse rate was 84, and the blood pressure was systolic 106 mm., diastolic 80 mm. The limbs, hands and feet were long and slender showing the characteristic spider-like extremities. The skeletal muscular system was poorly developed and hyperextensibility of the joints was present associated with apparently poor development of the ligamentous tissues. There was subluxation of the ankle joints. Absence of the subcutaneous fat was everywhere apparent. The genitalia were well developed. The arms were long, reaching almost to the knees. The measurements were as follows:

	PATIENT		NORMAL	
	inches	cm.	inches	cm.
Head	21.25	(54)	21.6	(55)
Chest	25.5	(65)	29.1	(84)
Waist	23.0	(58.42)	25.4	(64)
Span	66.25	(168)	62.1	(158)
Upper	32.25	(82)	29.9	(76)
Lower	31.25	(79)	30.8	(78)
Height	63.5	(161) lying down	60.7	(154)
Weight	61.75	(28 kg.)	92.9 lb.	(42 kg.)

The height was 61.25 inches (155 cm.) when standing due to the scoliosis which therefore reduced the height (Fig. 8). The roentgenograms were reported as follows:

Lateral Skull: The tables of the calvaria are of average thickness and there is no evidence of increased intracranial pressure and there is no unusual intracranial calcification. No demonstrable abnormality of bony development in the facial area. The sella turcica is shallow (Fig. 11).

Single Chest: No roentgen evidence of cardiovascular or pulmonary disease. There is noted, however, a moderate degree of scoliosis with the

FIG. 11. Case II. Lateral roentgenogram of the skull.

convexity in the lower dorsal level toward the right side (Fig. 12).

Both Hands: The bones of the digits and also the metacarpal bones are unusually long and the entire picture is suggestive of arachnodactylia (Fig. 13). The roentgenograms of the spine were reported as follows:

Lateral Spine: Segments of the spine, as seen in the lateral projection, are straight, there being loss of the normal lordotic curve in the lumbar level and a mild kyphosis is present in the dorsal level.

The laboratory studies made at Receiving Hospital were reported as follows:

Urinalysis: negative.

Glucose tolerance test:

Fasting 46 mg.
1 hour 111 mg.
2 hours 79 mg.
3 hours clotted.
4 hours 57 mg.
5 hours 32 mg.
6 hours 41 mg.

All urines negative for sugar.

Kepler water test: night specimen 26 cc. Largest day specimen 70 cc.

Blood urea: 34 mg.

FIG. 12. Case 11. Chest roentgenogram showing scoliosis of spine. The heart size was considered normal.

FIG. 13. Case 11. Roentgenograms of hands showing unusual length of digits and metacarpal bones.

Blood creatinine: 0.9 mg.
Kline reaction negative.
Kahn reaction negative.
Blood count: Red cells 4.7 million. Leukocytes 9,050, with a differential count of 61 per cent polymorphonuclears, 33 per cent lymphocytes, 4 per cent monocytes, 2 per cent eosinophils; hemoglobin 14 grams.

The visual fields were normal. No lens abnormality.

The follicle-stimulating hormone excretion was reported as 26 mouse units in twenty-four hours. The 17-keto-steroids were reported as 4.1 mg. per twenty-four hours. These values are normal for a fourteen year old boy.

COMMENT

In arachnodactyly the congenital defects are evident and certain data to be presented indicate that we are dealing with a primary pituitary defect which results in the target tissues, particularly the mesoderm, being defectively developed. Weve[13] called attention to the defect in the development of the mesoderm. Objection to this opinion is based on the fact that some of the typical ocular findings are in the ectodermal structures such as the lens and muscle of the iris. However, as we know, the supportive tissues in general and specifically in the eye, the vascular system, are mesodermal in origin and the lens and iris muscle depend for their support on this layer. Weve concluded that the syndrome is a congenital inherited entity which produces a mesodermal dystrophy. Concerning its etiology he said that all we know is that it is mostly an inherited condition. He was of the opinion that the eye weakness could be explained by primary mesodermal disturbances. The whole mesodermal layer partakes of the underdevelopment as shown by the aforementioned eye changes, the small slender bony structures with kyphoscoliosis, lax ligaments, small muscles, secondary anemia (mesodermal blood) small kidneys, small genitalia, lack of subcutaneous fat, poorly developed vascular system and dissecting aneurysms. Of importance is the underdevelopment and defect of the cardiovascular system which may be due to a primary pituitary disturbance.*

The high arched palate present in the 2 cases reported by Tobin and his associates as well as the high arched palate in the 2 cases herein reported and in both parents of the first case place this finding in a highly important etiological position.

This clinical finding of a high arched palate in each of 21 cases of retinitis pigmentosa was reported by Pino and me[7] and was subsequently verified by Givner and Bruger.[4] Gadbaw and I[6] gave further data concerning the significance of this finding. It was thought that the high arched palate indicated a pituitary disturbance and was related to the development of the pituitary and may be the result of abnormal embryological development of this gland. Most cases of arachnodactyly have a dolicocephalic head associated with a high arched palate. Mortimer[8] studied 494 cases of cranial dysplasia in human beings and concluded that 60 per cent of the patients who showed evidence of disturbance in cranial form and structure, presumably during the growth period, suffered subsequently at some time or another from a dyspituitarism that was recognized physiologically. As is known the pituitary develops from the roof of the mouth and there seems to be no question that the high arched palate and embryological development and function of the pituitary are etiologically related. Stockard and Johnson[10] in their studies on dogs with crossbreeding of various species found that: "The one character common to all breeds and hybrids in which structural misfits occur is an abnormality of the pituitary gland. Such an array of growth disharmonies in association with pituitary abnormality makes it seem highly probable that the pituitary secretions are largely concerned with the normal regulation and adjustment of growth among the organ systems and bodily parts. It should be remembered that many of these disharmonious arrangements are strictly inherited

* Work is now in progress in association with Dr. Louis Jaffe on the pituitary-vascular relationship.

in very definite fashion. This fact may mean that the related peculiarity of the pituitary is the primarily inherited character, while the structural derangements are secondary results due to the failure in harmonious growth regulation by the genetically modified pituitary gland." This would indicate that the pituitary gland is the primary factor in the development of the high arched palate. Most authors agree that the pituitary is the endocrine gland most frequently involved in arachnodactyly.

Tobin and his associates stated that the possible role of the endocrine glands in Marfan's syndrome has been debated repeatedly. There is no anatomic evidence, according to these authors, to implicate any of them but the pituitary. These changes are in the nature of an eosinophil hyperplasia. A deep sella was seen in the first case, and a hypopituitary type of glucose tolerance curve was seen in the second case. The curve was like that seen in hypophysectomized animals and in pituitary cachexia of humans.

The evidence points in the direction of a pituitary involvement. What is of interest is the finding of an eosinophil hyperplasia in several of the autopsied cases of arachnodactyly. This finding is usually associaated with overgrowth of tissues, such as in acromegaly and gigantism. Despite the eosinophil hyperplasia the clinical picture is unmistakably that of pituitary underactivity. Support for the opinion that eosinophil hyperplasia may be associated with pituitary hypofunction is found in mongolism. Benda's work[2] on mongolism helps to understand the eosinophil hyperplasia. His conclusions on this phase of mongolism are as follows:

> A study of the pituitary in mongolism reveals pathology which indicates that this condition is associated with abnormal pituitary function. In contrast to cretinism in which the pituitary tends to be enlarged the pituitary in mongolism is hypoplastic. Abnormally low secretory activity is indicated by (1) inability to produce secretory cells and granules and (2) by abnormal granule storage (stagnation) and disappearance of signs of secretory activity. In the first group, there is evidence of hypopituitarism with absence of these granule types which we have seen to be connected with all secretory activity. The gland fails to produce and store potent agents. In the second group the secretory elements are filled with one type of granule (alpha granules) while the beta cells regress to castration cells or delta cells (large chromophobes). The secretory chief cells (gamma cells) are underdeveloped. Mongolism is the congenital type of hypopituitarism.

That the clinical picture is one of hypopituitarism is evident and that the pituitary cells can respond is shown by the growth induced by testosterone as represented in the first case.

In epilepsy, migraine, and retinitis pigmentosa a high arched palate is common and, as noted, also in arachnodactyly. And like the latter disease the aforementioned diseases are associated with congenital defects such as hammer toes, spina bifida occulta, spinal deformities, cervical ribs and others.

Ulrich[12] studied 500 cases of migraine, and recorded the occurrence of a general disharmony in bodily development: premature graying of the hair, abnormal growth and distribution of hair, confluent eyebrows, convergent or divergent strabismus, asymmetric distribution of the pigment in the iris, myelinated nerve fibers in the retina, color blindness, irregular and abnormal development of the forehead, supernumerary nipples, small or undescended testicles, microcephaly with normal intelligence, cervical ribs and inequality of the breasts.

The fact that migraine, epilepsy, retinitis pigmentosa and arachnodactyly have a common denominator in the form of a high arched palate and malformations in bodily development indicates that there may be a common etiological factor. The embryological development of the hard palate, the pituitary gland, the hypothalamus and the optic system, also points to a common etiological factor in the produc-

tion of these diseases; at least speculation has been centered in these areas in a search for their etiology.

Duoparental inheritance factors in the case likewise point in the direction of the pituitary-hypothalamic area as the etiological factor. The fact that there were high arched palates in the patient and the parents, as well as shortness of stature in the asthenic type mother, diabetes mellitus in the maternal grandmother, epilepsy in a paternal cousin adds some force to the opinion that the pituitary was a prime factor in the production of arachnodactyly. It has been shown that the pituitary has a selective action on the mesodermal layer of the body. The accumulated data indicate that a defective pituitary will result in symptoms mainly found in the mesoderm. This would indicate that in arachnodactyly there is a congenital inherited pituitary-mesodermal defect.

The second case was in a Negro and this race has a peculiarity of the mesoderm. Several years ago I[5] showed that the mesoderm of the Negro was unique in many respects when compared with that of the white race. The Negro race's relative immunity to ectodermal, epithelial and nervous system disturbance was also emphasized.

A few examples of the unique character of the Negro's mesoderm are as follows:

It is a generally accepted fact that the Negro has a tendency to connective tissue overgrowth which predisposes him to keloids, fibroids, strictures, neurofibromatosis, and other connective tissue disturbances. The mesodermal hemopoietic system has a singular character in that sickle cell anemia is practically limited to this race. Furthermore pernicious anemia, thromobocytic purpura, and leukemia, are not common in the pure Negro.

The mesodermal blood vessels are attacked with undue frequency resulting in aneurysms (syphilitic and non-syphilitic), arteriosclerosis, and vascular disease in general. The lymphatic, osseous, and cartilaginous systems also show a predisposition to disease in the Negro. That the Negro also suffers not infrequently from arachnodactyly is shown by the report of cases by Futcher and Southworth;[3] Rambar and Denenholz,[9] and Baer, Taussig and Oppenheimer.[1]

The osseous system has certain similarities to eunuchoidism in which the extremities are long and slender and the epiphyses remain open for an abnormally long period. In the first case the span was 3 inches (7.5 cm.) greater than normal and the height 1½ inches (3.75 cm.). Within a period of approximately two months on a daily dose of methyl testosterone the height increased ¾ inch (1.8 cm.) and the span increased 2 inches (5. cm.).

In the second case the span was also approximately 4 inches (10 cm.) greater than normal and the height 3 inches (7.5 cm.) more than normal. Tobin's first case had grown 24 inches (61 cm.) in seven years, reaching a height at twenty years of 79 inches (200 cm.).

In the first case the mother was 61 inches (155 cm.) in height and weight 98 lb. (44.5 kg.), indicating an asthenic mesodermally weak individual. The maternal grandmother had diabetes mellitus, a disease in which the pituitary also plays a role. A paternal cousin had epilepsy.

SUMMARY

Two cases of arachnodactyly are reported. The first case was a six year old boy with subluxation of the lens and tremulousness of the iris (iridonesis). A congenital cardiac defect was assumed to be present. A large sella turcica was present. A response in height and weight to methyl testosterone took place within a period of two months. An increase in the output of 17-keto-steroids followed this therapy. The follicle-stimulating hormone output in both cases was normal.

The second case was in a fourteen year old Negro boy with no dislocation of the lens, a possible congenital cardiac defect, a marked increase in glucose tolerance; the curve was actually hypoglycemic like that

seen in pituitary cachexia or severe hypopituitarism.

A high arched palate was present in both cases and in the parents of the first case. This finding seems to be characteristic of arachnodactyly, and its significance in this disease as well as in migraine, epilepsy and retinitis pigmentosa associated with disharmonious bodily development was discussed. It was assumed to be related to the development of the pituitary, the anterior lobe of which originates embryologically from the roof of the mouth. This gland is probably an etiological factor in the production of arachnodactyly. The etiology may rest in a primary inherited pituitary disturbance and a secondary mesodermal tissue defect. The opinion that arachnodactyly is an inherited mesodermal defect is supported.

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THE QUANTITATIVE EVALUATION OF BONE DENSITY

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IN THE past the most common method for the appraisal of bone density and mineralization from roentgenograms has been by the subjective impressions of the roentgenologist or the research worker. An attempt was made by the senior author in 1927, and by Stein[8] and by Sanders[6] in 1937 to reduce skeletal mineral density evaluations to a somewhat objective basis through the use of a stationary beam of light passing through a certain area of a bone roentgenogram, also stationary, onto a photronic cell. The use of a static technique of this character, however, is attended by large variations, because the same anatomical position in the skeletal roentgenogram of the bone of different animals or human subjects, or of the same subject at different times cannot be located accurately by a stationary beam of light shining through a non-moving film.

In 1929 the senior author adapted a photographic tracing densitometer, built in the Department of Physics at The Pennsylvania State College for scanning spectrum photographs, to the problem of obtaining tracings of skeletal roentgenograms. At first, roentgenograms of the rat femur were traced, and later various bones of human subjects were evaluated by means of this instrument. Although a poor degree of reproducibility was obtained with this original instrument, particularly with any but large bones—because it lacked the refinements needed for precise results—its use demonstrated that the principle of making tracings from one landmark to another by means of a stationary beam of light and a moving film eliminated the basic difficulty with the static technique; namely, that of failing to locate the same area of the same bone roentgenogram twice in succession, or a comparable area in films of two or more bones.

In 1936, means became available to the senior author to procure a Type B Moll Recording Microphotometer from Holland; the instrument was designed for making tracings of spectral lines on photographic plates. A thermocouple served as the light-sensitive part of the apparatus, and this showed very slow response to changes of density as the film traveled through the beam of light. Other features of the instrument rendered it unfit in its original condition for the purpose of tracing roentgenograms of human beings and experimental animals. Through the technical assistance of Ernest Axman and of Warren Mack, the instrument was modified by the substitution of a photronic cell, and in many other respects. After two and one-half years of successful use of this device with roentgenograms of human subjects, Mack, O'Brien, Smith and Bauman[4] described the method as then developed.

From 1942 to 1949 the microphotometer and the general method of its use have undergone numerous further refinements, which have increased the precision and widened the range of bones which could be evaluated quantitatively; the method now is applicable to anything from the mouse femur to the skull of man, within a very small limit of error.

The accuracy of the microphotometric scanning procedure for evaluating the mineral density of animal and human bones depends upon the validity of two assumptions:

(a) *that the photographic density of the image on a roentgenogram is related in a known manner to the density of*

* Deceased October 20, 1945.

the mineral of the bone upon which the roentgenogram is based; and

(b) *that, through the use of a step wedge or ladder made of a substance of homogeneous density and generally similar in chemical composition to bone, placed on the film at the time when the exposure is made, corrections can be applied for unavoidable variations in exposure and development technique, within satisfactory limits.*

Quantitative measurements have been made on several thousand roentgenograms derived from living and cadaver bones of human and animal origin. In the Pennsylvania State College mass studies in human nutrition, conducted in the Ellen H. Richards Institute since 1935, the os calcis, the anteroposterior aspect of the foot, the hand, the elbow, and the knee are roentgenographed routinely. In certain longitudinal studies under the same auspices, the hip, the femur, the patella, the shoulder, and the skull are added to the routine series. From an evaluation of the foregoing, these conclusions may be drawn:

(a) The measurement of density of bone mineral by specially prepared roentgenograms can be accomplished with an error of only a few per cent. The method has a sound theoretical basis.

(b) Living bones act somewhat as reservoirs of calcium salts and take on or give up calcium compounds in accordance with the nutritional status of the individual, and other factors.

(c) Certain parts of certain bones react very quickly (within a few days) to changes in nutritional status, while other bone regions make relatively slow changes.

(d) Measurement of bone density in this way appears to have considerable promise as a clinical tool for determining the calcium nutritional status of an individual relative to the norm, and for detecting changes in calcium nutritional status caused by pregnancy, illness, change in diet, or other causes.

(e) The technique appears to offer significant advantages in medical research experimentation with mice, rats, and other animals, where it now is necessary to evaluate changes in skeletal status with time by killing part of the group periodically in order to make a chemical analysis of the bones. The present technique is suitable for bones even as small as those of mice, and would greatly reduce the number of test animals required in this type of work.

Preliminary to a discussion of the experimental technique, an outline of the pertinent theoretical considerations will be presented.

THEORETICAL CONSIDERATIONS

Roentgen-Ray Absorption. As is well known, roentgen radiation is absorbed in accordance with the relationships.

$$I = I_0 e^{-\mu x}, \tag{1}$$

where I_0 is the intensity of the beam of radiation striking the object, I is the intensity of the beam at some point located at a distance, x, inside the object, e is 2.718 . . . , the base of the system of natural logarithms, and μ is a quantity commonly referred to as the roentgen-ray absorption coefficient (linear).

The differential equation from which equation (1) is derived is:

$$\frac{dI}{Idx} = -\mu, \tag{2}$$

where it can be seen that μ also equals the fractional part of the intensity absorbed while the beam traverses a small distance, dx. Since the absorption results from the presence of atoms of an absorbing element in the path of the beam, the number of atoms encountered by the beam in a distance, dx, will be denoted by dn. Then, equations (1) and (2) can be written in another familiar form, in terms of n, the

number of atoms penetrated and μ_a, the atomic roentgen-ray absorption coefficient, as follows:

$$I = I_0 e^{-\mu_a n} \tag{1a}$$

$$\frac{dI}{Idn} = -\mu_a \tag{2a}$$

μ_a is equal to the fractional part of the energy absorbed on the average by one atom. In addition, a mass roentgen-ray absorption coefficient, associated with the absorption per unit mass of a particular substance, frequently is used. For the following discussion, it is most convenient to work with the atomic absorption coefficient, μ_a.

The Role of Scattering. Roentgen-ray absorption coefficients for most elements and wavelengths have been determined experimentally and are published in reference books. Several empirical formulas have been developed to express the absorption coefficient, in terms of the atomic number (Z) of the absorbing element, and the wavelength (λ) of the radiation. These expressions are of the form:

$$\mu_a = AZ + BZ^4\lambda^3. \tag{3}$$

The first term is the "scattering" term and the second term is known as the "fluorescent" or "true" absorption term. As the word "scattering" suggests, the first term in the absorption coefficient according to the classical definition does not represent absorption in the strictest sense of the word, but refers merely to a redirection or scattering of the radiation without important changes in the wavelength or energy. The second term represents true absorption of energy by the atoms involved.

The reason for including scattering in the classical definition of absorption can be seen from a consideration of the experimental apparatus used to measure the absorption coefficient. As indicated in Figure 1, a very sharp, pencil-like beam consisting essentially of monochromatic radiation is produced by the use of a filter and narrow slits; this is allowed to strike the specimen of which the absorption coefficient is to be determined. On the opposite side of the specimen there is placed a second series of slits, arranged colinearly with the first set of slits, together with a radiation detector. The ratio of I to I_0 is determined by comparing the detector readings with the specimen in place, and again not in place. The absorption coefficient then is computed from equation (1) or (1a). Only a very small amount of the total scattered radiation reaches the detector because of the slit system. This experimental procedure for measuring the absorption coefficient leads to the accepted value wherein the radiation scattered by the specimen and

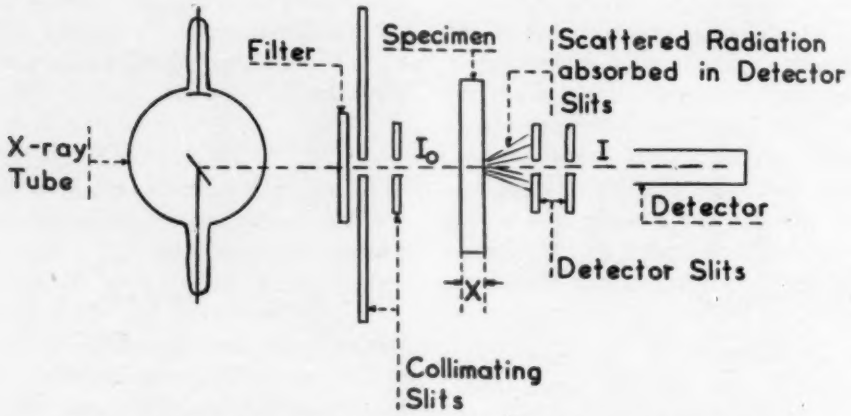

FIG. 1. Apparatus for measuring roentgen-ray absorption coefficient.

absorbed by the slits is considered to have been absorbed by the specimen. The procedure is most expedient because of the difficulty of collecting at a detector all or any known fraction of the scattered radiation.

When a roentgenogram of an object, such as a bone, is made, the radiation scattered from the various parts of the object is not absorbed by narrow slits, and a substantial part thereof falls onto the bone image, thus increasing its photographic density. The energy scattered from any particular portion of the bone is radiated in all directions, and the effect of the scattering is a general fogging or relatively uniform blackening of the film. The intensity of the roentgen radiation striking the film at any point on the bone image thus is greater than that which would be given by equation (1); and conversely, the thickness of the object, as calculated from measured values of I/I_0 and tabulated values of the absorption coefficient would be smaller than the actual thickness.

The scattering difficulty can be reduced in theory, and to a considerable extent in practice, by using radiation of a relatively long wavelength, or lower kilovoltage, so that the second term of equation (3), which is proportional to the third power of the wavelength, is very large in comparison with the scattering term, which is independent of the wavelength. A practical limitation arises from the higher radiation intensities and exposure time required for object penetration with low kilovoltage radiation. The scattering consideration may be of less importance where the absorbing specimen is composed of a chemical element having a high atomic number; but for such a specimen the practical necessity for using shorter roentgen-ray wavelengths to secure sufficient penetration may offset the discrimination against scattering afforded by the higher atomic number. As will be shown later, the technique under discussion includes an approximate correction for the effect of scattered radiation.

Comparison of Possible Techniques. At first glance, it might appear that measurement of roentgen-ray absorbing power for the purpose of determining the mineral density of living bones is not feasible. Bones are not uniform in density and have an irregular three-dimensional shape, with the result that measurements of mineral density on particular sample points of the bone cannot be reproducible or reliable as stated earlier. Instead, the present technique involves a measurement of the mineral density averaged over an entire bone cross-sectional area for which a microphotometric tracing of the roentgenogram is made. The averaging procedure which takes place automatically when a trace is made between defined landmarks on the bone image by a stationary beam of light through a moving film disposes of the reproducibility difficulty inherent in the stationary beam—stationary film technique. In the latter, the relative positioning of the roentgen tube, the bone, and film, together with the location of the light spot on the bone image cannot be controlled with sufficient accuracy to insure that the mineral density at specified penetration positions in different bones or in the same bone at different times can be compared with any reasonable significnce.

In order to determine the mineral density from the number of atoms which the roentgen-ray beam has penetrated, it is necessary to measure I/I_0 for substitution into equation (1a). There are three general types of apparatus available for the detection and measurement of roentgen radiation. These are the ionization chamber, the fluorescent screen, and the photographic plate or film. Although the ionization chamber is conceded to be the most suitable device for the quantitative measurement of roentgen-ray intensity, it presents considerable experimental difficulties if one desires to obtain the average absorption of a considerable portion of bone; in the latter case, the bone to be measured would have to be placed successively in a large number of different and accurately controlled positions relative to the roentgen-ray beam going from the

tube into the ionization chamber, and it would be necessary to record the ionization chamber current for each of these positions. In addition to the difficulty of acquiring such data with living human or animal subjects, this method does not provide as complete and detailed a permanent record as would be desired.

The second device, the fluorescent screen, does little more than make an instantaneous conversion of the roentgen-ray

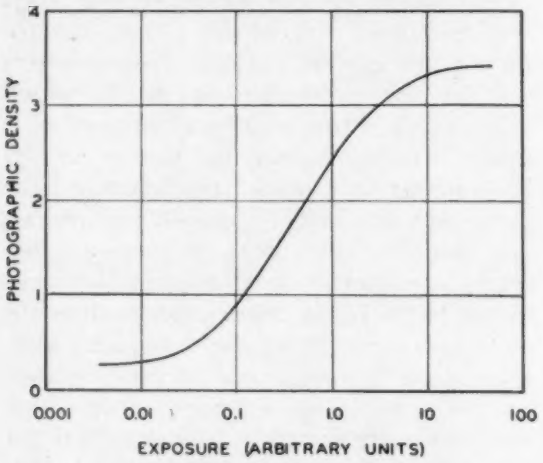

FIG. 2. A typical Hurter and Driffield (H and D) characteristic for photographic film.

image into a corresponding image of visible light, This visible image, if produced in a darkened room, could be scanned with a photoelectric device, and essentially the same data could be derived therefrom as with the ionization chamber method. Another variation would consist of photographing the fluorescent screen and evaluating the photograph at leisure. Use of the fluorescent screen in this way offers the possibility of simultaneous visual observation and permanent photographic recording of the data, although detail in bone density might be sacrificed to a certain extent by this technique.

The third detecting device, roentgen film, is known to possess certain characteristics not suited to a quantitative measurement of stimuli, without the application of special techniques. The roentgenographic technique is well understood and widely used in the medical profession, however, and offers the additional advantage of providing a detailed and permanent record of the bone. The direct roentgenogram resembles the photograph which might be taken of the roentgen-ray energized fluorescent screen. All of the experimental work in connection with the present technique has been carried out by direct roentgen-ray exposure of the bone image on standard non-screen roentgen film, and the following discussion will relate primarily to this particular method, although in many instances the analysis will be directly applicable to the other possible methods mentioned above.

Analysis of a Technique Using Roentgen Film. A technique in which the blackening of a photographic plate or film is to be used as a quantitative measure of exposure requires the establishment of some procedure for determining the sensitometric curve of the plate or film, also known as the Hurter and Driffield Characteristic. This relationship varies so greatly with development and exposure conditions and with the particular emulsion that it has been found necessary to make a separate determination of the sensitometric curve for each film used to measure exposure values quantitatively. The curve of photographic density or blackening versus exposure is of the general shape of the Hurter and Driffield (H and D) curve shown in Figure 2; the nearly horizontal position of the curve occurring at low density levels corresponds to the situation in which the density approximates that of the unexposed film base, and the exposure is not sufficiently great to exercise appreciable effect upon the emulsion. The nearly horizontal portion of the curve occurring at a high density value is associated with exposures sufficiently long to expose the emulsion so completely that further increases in exposure cause little increase in density.

It is important, in using film to measure intensity or exposure, to keep the exposures on the comparatively straight central portion of the Hurter and Driffield curve, in

order that a small variation in exposure will show up as a measurable change in photographic density. If the range of exposure is very small, it often is sufficient to consider the curve to be a straight line. In the latter case, determination of the slope of the curve at the midpoint of the exposure range may suffice for measurement of exposure ratios. Most roentgenograms of bones, however, involve a wide range of exposure. Hence, it becomes necessary to construct a major portion of the sensitometric curve in order to make measurements of exposures. As will become apparent, the operation of correcting for the sensitometric curve can be combined with several other correction operations with an economy of labor and complexity.

Equation (1a) can be written also in the form:

$$n = \frac{1}{\mu_a} \ln_e \left(\frac{I_0}{I} \right), \tag{4}$$

where n represents, as before, the number of atoms in the path of the beam. If the continuous spectrum roentgen radiation generated by standard medical equipment is employed, I_0 and I will involve radiation of many different wavelengths, λ, for each of which a different μ_a value, as given approximately by equation (3), will apply. In fact, as the continuous or white radiation penetrates an object, its spectrum shape changes considerably because the softer or longer wavelength roentgen rays in the spectrum undergo more absorption, as is indicated by equation (3). As a result, the overall rate of absorption becomes greatest near the exposed surface where there is a large proportion of long wavelength radiation in the beam, and diminishes as the radiation penetrates farther into the absorbing object. In addition, if the average density of the bone is to be evaluated, procedure must be found to take into account the general non-uniformity of bone density, which causes $\rho(x)$, the atomic density, or number of absorbing atoms per cubic centimeter of bone to vary with the distance of roentgen-ray penetration. Fortunately, these difficulties can be resolved by the following procedure, which allows quantitative determination of bone density from roentgenograms prepared with standard continuous spectrum roentgen-ray machines of the type commonly used in medical work.

Let the bone of which the density is to be determined be exposed on the roentgen film, and at the same time let there be exposed for reference purposes a wedge-shaped object of known dimensions and chemical composition. Figure 3 shows a cross sectional view of the roentgen tube, the bone, the wedge, and the roentgen film. The position of the cross section is defined by the tracing path on the film and the focal spot of the roentgen tube.

For the time being it is assumed that the roentgen rays are monochromatic or of single wavelength, and that the bone and wedge both are comprised of a single absorbing element. It is assumed, also, that the roentgen tube is sufficiently far from the absorbing objects that the wave front essentially represents a plane. Referring now to equation (4), I_0 is taken to be the intensity of the radiation incident upon the top of the bone and wedge, and I is taken to be the intensity of the beam emergent from the bone or wedge and striking the roentgen film. Moreover, n represents the total number of absorbing atoms encountered by the roentgen-ray beam in passing through the bone or wedge. Referring again to Figure 3, $f_1(x)$ and $g_1(x)$, respectively, represent the top boundary curves of the bone and wedge, and $f_2(x)$ and $g_2(x)$ denote the corresponding bottom boundary curves. For convenience, the length of the roentgen-ray path through the bone cross section is represented by $F(x)=f_1(x)-f_2(x)$ and the length of the radiation path through the wedge by $G(x)=g_1(x)-g_2(x)$. The density of the bone cross section, expressed in atoms of absorbing element per cubic centimeter, is denoted by $\rho(x,y)$; note that this quantity depends both upon the x and upon the y coordinates of the point on the bone cross section at which it

is evaluated. The wedge is assumed to be perfectly uniform in atomic density, which is denoted by ρ'.

From the definition of n, for the bone image at the point, x,

$$(5) \qquad n(x)=\int_{f_2(x)}^{f_1(x)}\rho(x,y)dy=\bar{\rho}(x)F(x),$$

and for the point x' on the wedge image,

$$(6) \qquad n'(x')=\rho'G(x).$$

The notation, $\bar{\rho}\,(x)$, denotes the average tracing path a point, x', on the wedge image having the same blackness or density can be found, then, for these corresponding points,

$$(9) \qquad I(x)=I'(x'), \quad \text{and}$$

$$(10) \qquad \mu_a\bar{\rho}(x)F(x)=\mu_a'\rho'G(x')$$

$$(11) \qquad \bar{\rho}(x)=\frac{\mu_a'G(x')}{\mu_aF(x)}\rho'.$$

Equation (11) states that the atomic density of the bone, averaged along the

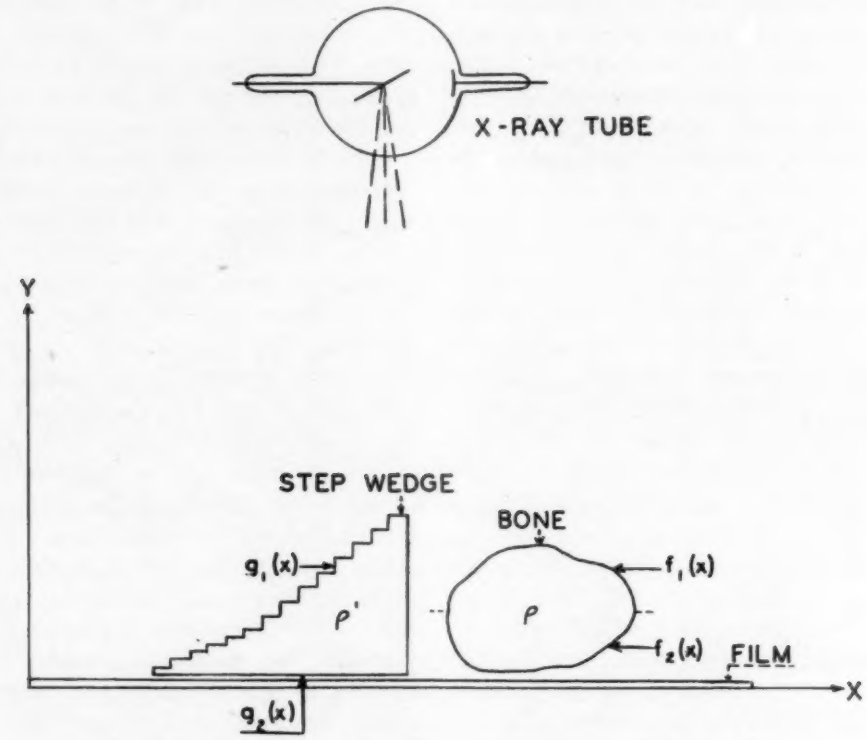

FIG. 3. Schematic diagram of roentgen tube, wedge, bone and film.

atomic density along the roentgen-ray path.

From equation (1a) the roentgen-ray intensity incident on the film under the bone at the point, x, is

$$(7) \qquad I(x)=I_0e^{-\mu_a n(x)}=I_0e^{-\mu_a\bar{\rho}(x)F(x)},$$

and under the wedge at the point, x', is

$$(8) \qquad I'(x')=I_0e^{-\mu_a n'(x')}=I_0e^{-\mu_a'\rho'G(x')}.$$

If for any point, x, on the bone image path of the roentgen-ray beam, equals the corresponding atomic density for the wedge, multiplied by the ratio of the absorption coefficient of the wedge atoms to the absorption coefficient of the bone atoms, and also multiplied by the ratio of the path length in the wedge corresponding to the point x' to that in the bone for the point, x.

Up to this point in the discussion, it has been assumed that the illuminating roent-

gen rays are monochromatic and that there is only a single absorbing element both in the wedge and in the bone. Equation (11) is subject to these two limitations, which will be considered next.

If the illuminating roentgen radiation is of the continuous spectrum type, validity of the above analysis requires that $I(x)=I'(x')$ for every wavelength in the spectrum. Because the sensitivity of emulsions varies with wavelength, points of equal photographic density on the two images do not necessarily arise from equal roentgen radiation intensity unless the spectral distribution is the same for the two points. Consequently, the expression, $\frac{\mu_a'G(x')}{\mu_aF(x)}$ must have the same value for all wavelengths in the spectrum. $\frac{G(x')}{F(x)}$ is determined only by the physical dimensions of the absorbing objects and is independent of the wavelength, λ. The factor μ_a'/μ_a, however, will depend upon λ unless one of the following provisions is met: (a) the absorbing element in the wedge is the same as the absorbing element in bone, whereupon $\mu_a'/\mu_a=1$; (b) the roentgen-ray spectral distribution and the absorbing element in the wedge are so chosen that the scattering absorption is negligible compared to the fluorescent absorption both in the bone and in the wedge, whereupon

$$\frac{\mu_a'}{\mu_a}=\frac{B'Z'^4\lambda^3}{BZ^4\lambda^3}=\left(\frac{B'}{B}\right)\left(\frac{Z'}{Z}\right)^4,$$

as indicated by equation (3); and (c) the spectral distribution and the absorbing element in the wedge are so chosen that the fluorescent absorption is negligible compared to the scattering absorption both in the bone and in the wedge, whereupon:

$$\frac{\mu_a'}{\mu_a}=\frac{A'Z'}{AZ}.$$

In the present technique, the first condition is satisfied essentially, since μ_a'/μ_a is made independent of wavelength for any spectral condition by using ivory for the wedge so that calcium is the principal absorbing element both in the bone and in the wedge. The second condition is satisfied also within a close approximation by the use of a continuous roentgen-ray spectrum having a short wavelength limit sufficiently great that scattering absorption is relatively small.

The second assumption, that there is only a single absorbing element in the bone and the wedge, will now be considered. Let there be m absorbing elements appearing in the bone or in the wedge, or in both. Since the roentgen-ray absorbing properties of an atom are essentially independent of its state of chemical combination equation (10) can be generalized as follows:

$$(12)\qquad \sum_{k=1}^{k=m}[\mu_k\bar{\rho}_k(x)F(x)]=\sum_{k=1}^{k=m}[\mu_k\rho_k'G(x')]$$

In this equation, subscript k denotes the k'th absorbing element. In connection with the problem of determining the density of living bones from roentgenograms, it is of interest to consider the effect on determination of the density of calcium, the principal absorbing element both in bone and ivory, of the presence of incidental absorption due to other elements. Let $k=1$ for calcium. Then, if the calcium determination is to be correct, as given in equation (11),

$$(13)\qquad \bar{\rho}_1(x)=\frac{G(x')}{F(x)}\rho_1'.$$

Subtracting equation (13) from equation (12),

$$(14)\qquad \sum_{k=2}^{k=m}\mu_k[\bar{\rho}_k(x)F(x)-\rho_k'G(x')]=0.$$

Equation (14) is satisfied by

$$(15)\qquad \bar{\rho}_k(x)=\frac{G(x')}{F(x)}\rho_k'$$

for any value of wavelength. This result indicates that, in order for equation (13) to hold for any value of λ, other absorbing

elements present must be found in the same proportion to calcium in the bone as in the wedge. Adherence to this condition cannot be established conveniently for living bones, that is bones in living human beings or animals, where it is not practicable to determine the proportion of other elements for a specific bone with great accuracy. It is of interest to return to the case where scattering is very small.

It can be shown by expansion from equations (3) and (12) that, for the case where scattering is very small,

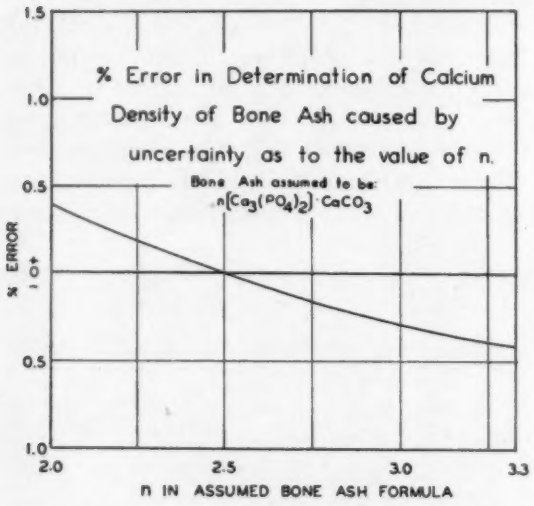

FIG. 4. Percentage error in determination of calcium density of bone ash.

$$\bar{\rho}_1(x)\left[1+\frac{\sum_{k=2}^{k=m} B_k Z_k{}^4 \bar{\rho}_k(x)}{B_1 Z_1 \bar{\rho}_1(x)}\right] \cong \frac{G(x')}{F(x)}\,\rho_1'\left[1+\frac{\sum_{k=2}^{k=m} B_k Z_k \rho_k'}{B_1 Z_1 \rho_1'}\right]. \tag{16}$$

This equation allows an approximate correction to be made for differences in atomic composition between the bone and the wedge. The value of ρ_1', ρ_2', ρ_3', . . . can be found from chemical analysis of the wedge material; this will fix the value of the bracketed expression on the right side of equation (16). The value of $\bar{\rho}_1(x)$, $\bar{\rho}_2(x)$, $\bar{\rho}_3(x)$, . . . cannot be determined for living bones and must be assigned median values estimated from chemical analysis of cadaver bones.

Although there is considerable controversy in the literature concerning the chemical structure of bone, there is reasonably good agreement on the atomic composition, that is, the relative quantities of each element. For purposes of determining the composition by elements, the following approximate formula is satisfactory for bone ash:

$$n[Ca_3(PO_4)_2]:CaCO_3 \qquad 2 \leqq n \leqq 3\tfrac{1}{3}.$$

For $n=2.5$, calcium is responsible for 79.60 per cent of the true absorption, phosphorus for 14.8, oxygen, 5.5, and carbon approximately 0.1 per cent. It is seen in Figure 4 that use of the median values for $\bar{\rho}_1(x)$, $\bar{\rho}_2(x)$, $\bar{\rho}_3(x)$, and $\bar{\rho}_4(x)$ corresponding to $n=2.5$ leads to less than 0.5 per cent error in the determination by true roentgen-ray absorption of the calcium density of bone ash within the expected range of variation of n.

Organic material in bone, including ossein and fat, is about 35 per cent of the total bone weight. This material is composed chiefly of carbon, oxygen, and hydrogen atoms which have smaller atomic numbers than the calcium and phosphorus in bone ash and thus have relatively small true absorption coefficients. The true absorption from this material has been estimated from equation (3) to be about 2 per cent of the true absorption occasioned by the bone ash. The classical scattering absorption, as estimated from equation (3) for the organic material, is considerably larger. Most of the scattered radiation is recovered, however, with the result that, for the roentgenographic technique under discussion, the effective absorption of the organic material is small as compared with that of the bone ash. This relationship has been verified experimentally for cadaver bones and will be the subject of further reports.

The absorption of roentgen radiation by

flesh and soft tissue is a possible source of error in the evaluation of the density of living bones by this technique. The relative absorbing power of the flesh and soft tissue is considerable under some conditions, and depends on the age of the subject, the identity of the bone cross section, and the roentgen-ray wavelength. There are some bones, such as the os calcis, where the flesh is comparatively thin and has relatively small absorptive effect. For most round bones, a simple correction can be made for flesh absorption. Specific procedures which have been developed for making flesh corrections will be described in a forthcoming report.

The various roentgen-ray absorption laws which have been cited above and which form the theoretical basis for this technique may be found in most text books on roentgen rays. The readers are referred to Clark[1], Compton,[2] Sproull,[7] and Terrill and Ulrey[9] for more rigorous statements of these laws and the limits of their applicability.

EXPERIMENTAL TECHNIQUE

Because of the difficulty of attaining high precision in locating the bone and film with respect to the roentgen tube when the roentgenogram is taken, and in locating a small spot on the film image after development, the only practical procedure is to consider not the blackness of a single spot on the bone image but instead the photographic density averaged along a linear path on the image, which represents the bone material found in a cross section of the bone along this path. This path is traced with a recording microdensitometer, and a record is secured of the photographic density as a function of the distance along the tracing path, as shown in Figure 5. Figure 6 shows the roentgenogram corresponding to Figure 5. Note that two dots are used to align the film in the microphotometer. The mineral density value obtained from analysis of a densitometer trace is the average mineral density over the cross-sectional slice of the bone defined by the tracing path, by the position of the roentgen tube at the time of exposure, and by the width of the densitometer slit opening transverse to the tracing path. This width, which is about 1 millimeter, corresponds to the thickness of the cross-sectional slice.

On the basis of experience and experimental convenience, certain selected tracing paths have been found suitable for particular purposes, and considerable care has been taken to devise standardized methods for securing uniform positioning of the bone at the time of taking the roentgenogram, and for standardizing the position of the tracing path on the film. Because the mineral density is averaged over a considerable portion of the bone volume, and because the exposure and tracing positions are carefully standardized by reference to landmarks on the bone, it is possible to reproduce mineral density values, as evaluated for the same slice of the same bone from different films, with an accuracy of a small percentage. The principal tracing paths which have been studied to date are indicated on Figures 7 and 8, although numerous others are possible.

Either a long bone, or one of the round bones serves as a subject for evaluation of mineral density indices. Certain of the long bones have been found to change during periods of certain types of undernutrition with respect to the mineral density, first at the bone metaphysis, and later in other regions. Changes are found in the width of the marrow cavity, if any, and in the density of the skeletal material itself. Such round bones as the os calcis, the ossific centers of the wrist, the patella, and others, change in mineral density with certain changes in nutritional or pathological status. The mineral density changes are believed to be essentially quantitative, without involving material alterations in the chemical composition of bone mineral.

In making roentgenograms, roentgen film of the double-coated acetate base type is used. It is necessary to employ a plumb bob or rod for locating the roentgen tube with

respect to a standard position over the part of the body being filmed, and to use a highly standardized technique of exposure and development. Tube voltages between 45 and 55 kilovolts have been found satisfactory for most work.

The following gives the essential steps involved in taking a roentgenogram and in making and evaluating a densitometer trace by the microphotometric method, using Model 4 in the series of microphotometers which have been developed since this type of measurement first was undertaken by the senior author:

Step (1). The roentgen film is made in a standard position for any part of the body which is to be used, employing an exposure energy suitable to the thickness of the object examined. A calibrated ivory step wedge is used in a standard position on each film. This is called *Film A*. A second film is taken at right angles to the first,

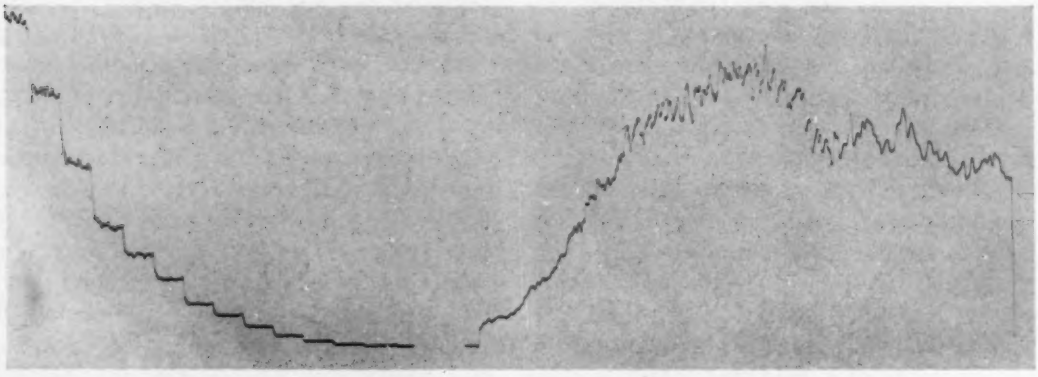

FIG. 5. Densitometer trace of os calcis.

FIG. 6. Roentgenogram for densitometer trace of Figure 5.

called *Film B*. After exposure, the films are developed, fixed, and washed under as nearly uniform conditions as can be achieved.

Step (2). A contact positive is made from Film A, which is the film from which microphotometric tracings are made. In order to secure maximum reproducibility of data, systematic procedures have been evolved for establishing the exact position of the axes of the bone image along which the densitometer traces are made. The positive is used for locating tracing paths without damage to the roentgen film itself. The ends of the tracing paths then are defined on the film by means of small ink dots outside of the traced region.

Step (3). Tracings are made along the predetermined path or paths on the film, both through the bone and ivory wedge images.

Step (4). Each bone tracing is divided into a finite number of segments in accordance with a standardized procedure.

Step (5). The area under each segment of the trace is measured by means of a planimeter.

Step (6). The heights of the definable steps in the wedge tracing are measured.

Step (7). An interpolation formula is used to correct the average trace height of each segment of the bone tracing for exposure and development deviations in terms of observed height of trace and measured physical thickness of the adjacent steps on the ivory standardization wedge. The corrected segment trace heights then may be averaged to obtain a corrected average trace height value for the entire trace, expressed in units of centimeters of equivalent ivory thickness.

Step (8). Linear measurements are made both on Film A and on Film B, which enable the cross-sectional area of bone corresponding to the tracing path to be estimated. The probable cross-sectional shape of the cross sectional bone area is determined from measurements on Films A and B and from a study of cadaver bones.

Step (9). The corrected equivalent ivory

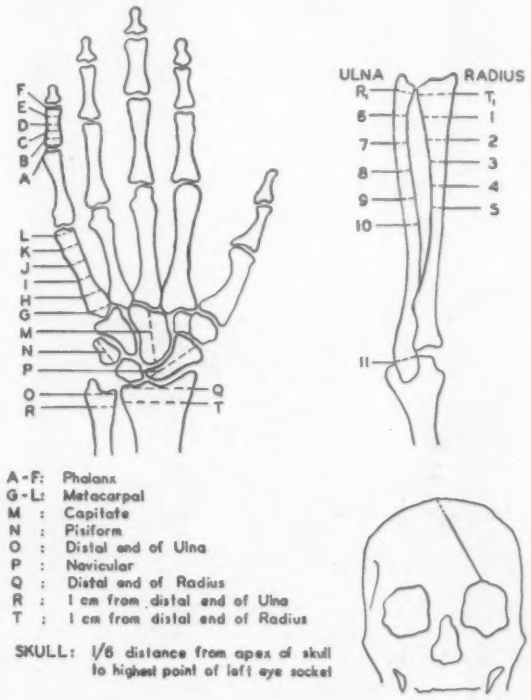
ULNA
RADIUS
A-F: Phalanx
G-L: Metacarpal
M : Capitate
N : Pisiform
O : Distal end of Ulna
P : Navicular
Q : Distal end of Radius
R : 1 cm from distal end of Ulna
T : 1 cm from distal end of Radius
SKULL: 1/6 distance from apex of skull to highest point of left eye socket

Fig. 7. Bone tracing paths.

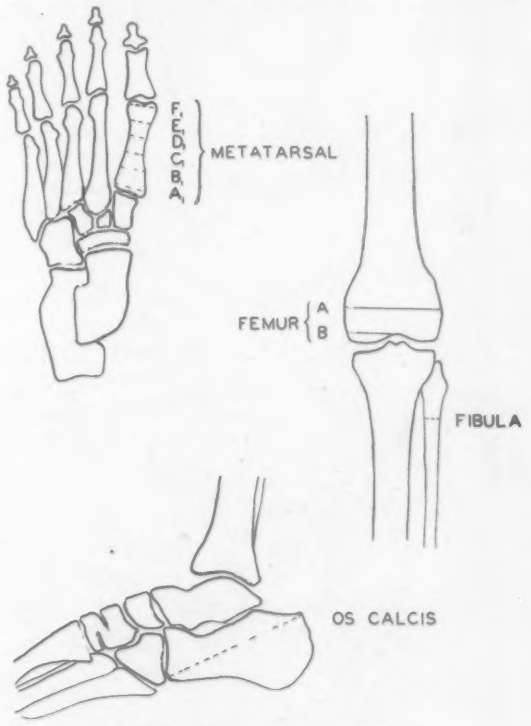

Fig. 8. Bone tracing paths.

thickness of the trace is divided by the estimated average physical thickness of bone corresponding to the microphotometer tracing path, and multiplied by the density of ivory in grams per cubic centimeter. The result is the IVORY DENSITY of the bone in grams of equivalent ivory per cubic centimeter of bone. A factor giving the ratio of bone density to density of the specific ivory wedge enables the result to be reported as bone density in grams of bone ash per unit volume.

Step (10). In certain studies Steps (8) and (9) are omitted for simplicity, and the result is expressed in terms of the average equivalent ivory thickness, in centimeters, for the bone cross section.

A precision microdensitometer, or microphotometer used in this technique, Model 4 as mentioned above, is illustrated in Figure 9; this functions essentially as follows:

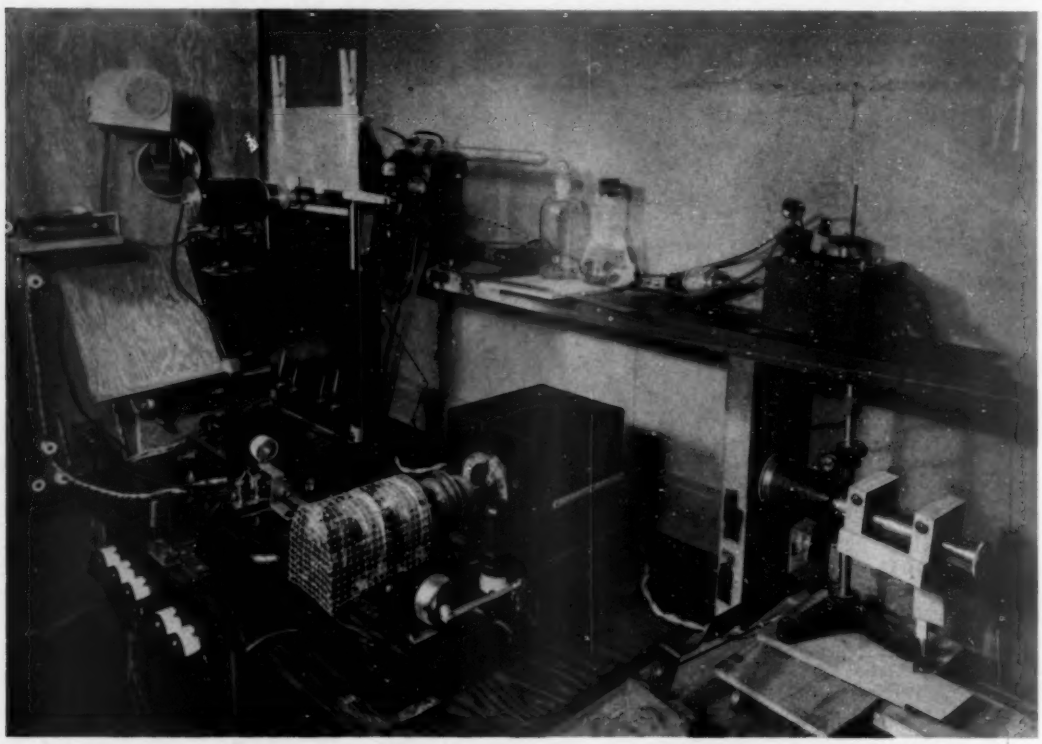

FIG. 9. Photoelectric microdensitometer (Model 4) used in making photographic tracings of mineral density in bones. (Note: Galvanometer stands at right outside of the field of the photograph.)

A stationary beam of light passes through a lens condensing system, thence through the roentgenogram, and finally onto a photronic cell. The condensing system focuses the image of a straight filament lamp through the roentgen film and onto the photronic cell, the latter of which is in a light-tight box. The image of the brightly illuminated roentgen-ray area is focused on the plane of an adjusting slit on the near side of the photronic cell, and thence onto the cell. The latter is connected directly with a sensitive galvanometer.

The film being scanned is mounted on a carriage which moves at a constant velocity of approximately 0.01 inch per second past the scanning beam. The carriage is moved by the same synchronous motor which turns the drum on which the photographic recording paper is placed. This assures a constant ratio between the linear

velocities of the carriage through the scanning beam and the surface of the recording paper. The instrument thereby is a recording densitometer.

It is essential that the intensity of the scanning lamp be controlled as closely as possible. It is operated in a direct current circuit designed to provide adequate control of the voltage across the lamp.

lens mounted so that its axis is perpendicular to the long dimension of the paper. Light is supplied to the galvanometer mirror by a suitable lamp-lens-slit system.

The height of the tracing increases with the light transmitted through the corresponding point on the roentgen film, which in turn is a determinable function of the amount of mineral matter through which

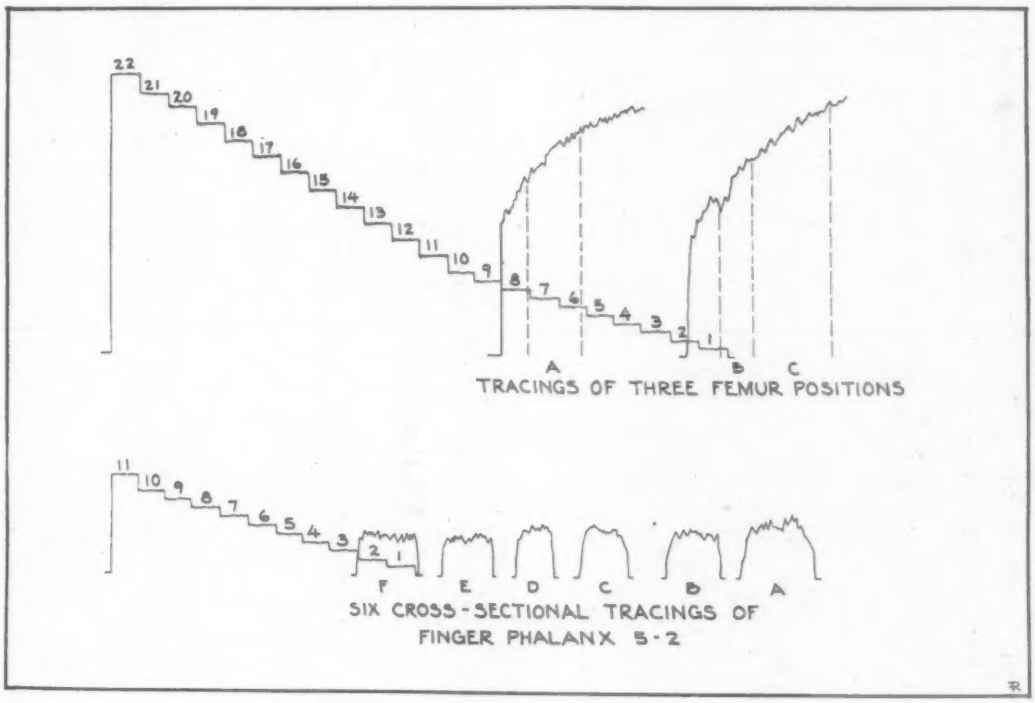

Fig. 10. Representative corrected microdensitometric bone tracings from roentgenograms (above) of three femur positions, and (below) of six cross-sectional finger phalanx 5-2.

The microphotometer must be operated in a dark room. It is convenient to use a second dark room for the processing of the photographic recording paper. The suite of laboratories used at the Ellen H. Richards Institute at present is located on a subbasement floor in a building in which freedom from external vibration is provided.

The drum accommodates recording paper up to 12 by 40 centimeters and is mounted in a housing which is light-tight. Light from the galvanometer mirror is admitted through a slot and brought to a focus on the surface of the paper by a cylindrical

the roentgen radiation has passed during exposure of the film. The area of the cross section (estimated from two exterior measurements of the bone) multiplied by the width of the path scanned on the roentgenogram image by the densitometer give a close approximation to the volume of bone for which the average mineral index is evaluated. No bone position is traced except those for which cadaver bones have been studied to assist in estimating bone shapes in directions other than the two for which roentgenograms (Film A and Film B) are taken.

Experimental checks on the reproducibility of the technique have been carried out by evaluating the Mineral Index from a number of roentgenograms prepared at the same time for the same bone under varying conditions of exposure and development. Figure 12 indicates the result of a typical series of tests in which seven identically exposed films of the ulna of a same film does not vary greatly over the wide range of development conditions considered.

It is important, however, that the exposure and development conditions be such that no part of the bone image lies either in the fog or in the black density saturation regions of the film characteristic curve, as illustrated in Figure 2, which was presented

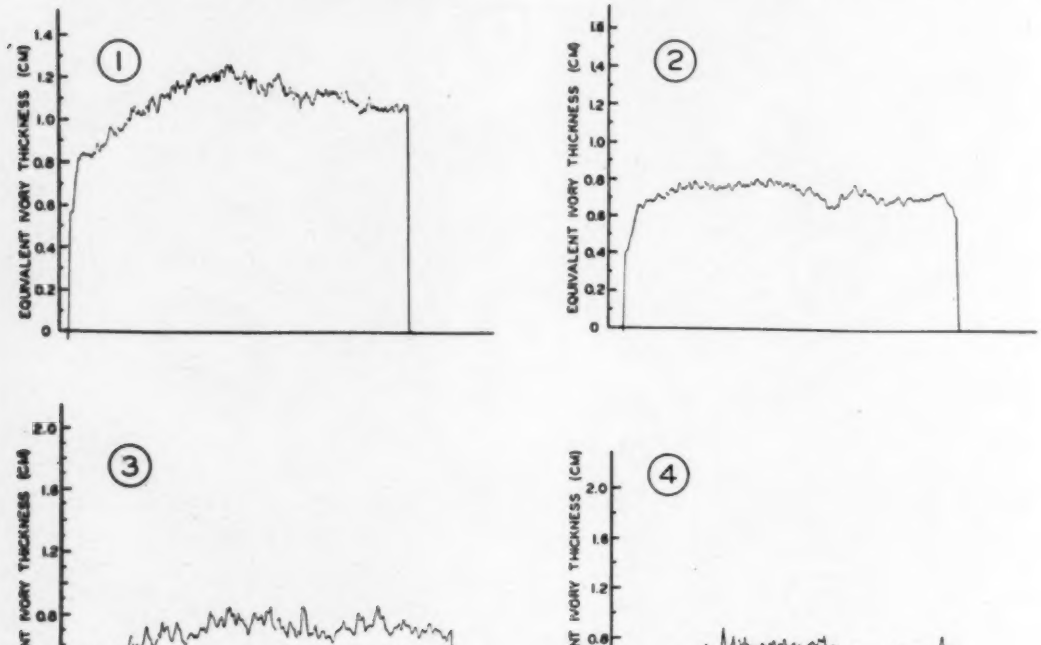

FIG. 11. Representative micro-densitometric traces of the os calcis of 4 children: (1) a well nourished male 4 years, 10 months, 8 days; (2) a slightly undernourished female 3 years, 10 months, 11 days; (3) a female transverse myelitis subject 10 years, 1 month, 12 days; and (4) a female 10 years, 10 days diagnosed as having psathyrosis (dysplasia of bone and cartilage).

child were developed for different periods ranging from two to four and a half minutes. The curve labeled A shows a wide variation with development time of the Mineral Index value which might be computed on the basis of film density alone. The curve labelled B shows that the corrected Mineral Index, obtained by correcting the density of the bone image for each film on the basis of the photographic trace of the ivory step-wedge images on the to show a typical Hurter and Driffield characteristic for photographic film.

A semi-automatic film evaluating machine of novel design (Model 5 in the Ellen H. Richards Institute series) has been constructed by the second-named author, and now is in routine use. As indicated in Figure 13, this machine comprises a densitometer, two pen and ink recorders, a function transformer, and an integrator. A trace of the ivory step-wedge image is made

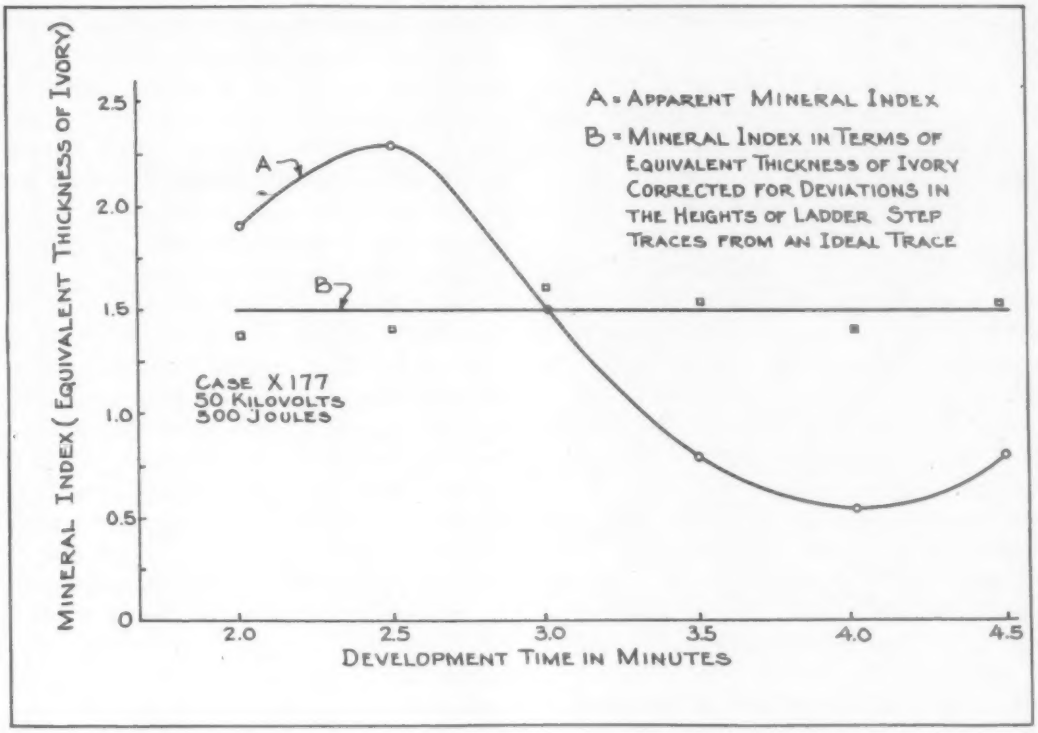

Fig. 12. Development time series on ulna.

first for each film, using the microdensitometer and first recorder, in order to determine the functional relationship between densitometer deflection and equivalent ivory thickness for that film. These data are fed manually into the function transformer. The desired bone image paths on the film then are traced. The second pen and ink recorder and the integrator are actuated continuously during the bone tracing process by the function transformer, in order to provide a corrected

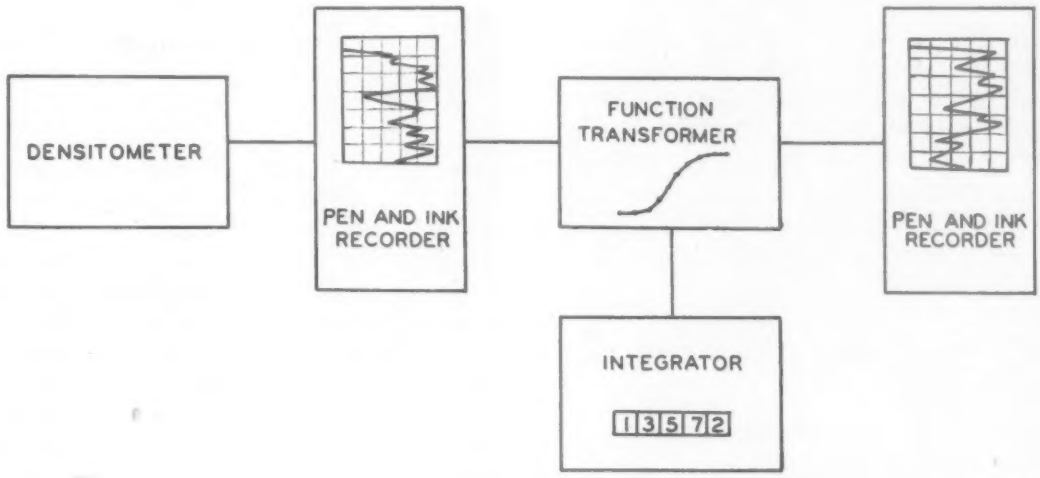

Fig. 13. Film evaluating equipment (Model 5).

equivalent ivory thickness trace and a corrected ivory cross sectional area, respectively, for the bone. The latter value, multiplied by the density of ivory and divided by the estimated bone cross sectional area gives the IVORY DENSITY of the bone, which in turn can be converted to BONE DENSITY as mentioned above.

The following gives the essential steps involved in making and evaluating roentgenograms by the semi-automatic method, using the Model 5 machine under discussion.

Steps (1) and (2). These steps are the same as those given for the Model 4 machine.

Step (3). A tracing is made along the ivory wedge image on the film.

Step (4) The heights of the definable steps in the wedge tracing are measured.

Step (5). The data obtained in (4) above are set manually into the function transformer by an operator, in order to establish the functional relationship between densitometer deflection and equivalent ivory thickness for the film being evaluated.

Step (6). The desired tracings are made along bone paths.

Step (7). During the bone tracing process, the second recorder is producing a trace, transformed automatically from the densitometer trace by the function transformer, of equivalent ivory thickness versus distance along the tracing path. Concurrently, the equivalent ivory thickness is integrated automatically along the tracing path to give a numerical value for the equivalent ivory cross sectional area of the portion of bone traced. The average equivalent ivory thickness of the cross section then is obtained by dividing the equivalent ivory cross-sectional area by the length of the tracing path.

Steps (8), (9), and (10). These steps are the same as those given above for the Model 4 machine.

APPLICATIONS

The technique described has numerous applications, many of which have not been evaluated fully as yet. In medical research studies, where measurement of the density of living bones, particularly human, is necessary, the technique should be of great utility. As a clinical tool for use in evaluating the nutritional status of an individual relative to the norm, the technique has proved in these laboratories to be of inestimable value. Comparison of successive measurements on the same individual provides a sensitive means of detecting any change in bone mineralization occasioned by changing nutritional status, by illness, or by pregnancy, and of determining the need for dietary supplements or special medical care. It is anticipated that the rate of mending of fractures or breaks can be investigated quantitatively with the help of this technique, either for medical research or for routine treatment purposes. Preliminary work indicates that quantitative study and observation of arthritic and joint calcification conditions may prove worthwhile. Soft tissue calcification following injury has been studied by this technique, as has been senile demineralization.

Aside from its applications to measurement of bone density, the technique may also be applied to quantitative measurement of the roentgen-ray absorbing power of soft tissue and flesh. Roentgen-ray absorption depends upon the chemical composition as well as upon the quantity of the material penetrated. For bone, the chemical composition is known within close limits and the density can be determined by roentgenographic means. For flesh or soft tissue the composition is not known generally, and density determination is thus not feasible. The technique as described, however, involving a recording densitometer and a standardizing step wedge, permits the average roentgen-ray absorbing power of the flesh or soft tissue associated with any selected region of a roentgenogram to be measured quantitatively in units of centimeters of equivalent ivory thickness; this gives satisfactory comparative results. Later, studies on the chemical composition of mineral deposits

in soft tissue may enable such microdensitometric measurements to be made in terms of density of actual mineral compounds.

It is well known that a modern, carefully designed densitometer is many times more accurate than the human eye for evaluating the density of photographic film. In view of this fact and of the virtual elimination of exposure and development variations effected by use of the step-wedge following the technique as described herein, it appears that the subject technique may provide a valuable tool for use by roentgenologists. A possible application of the technique to tracing injected materials in human beings and animals also exists. Where the chemical composition of the injected absorbing substance is known, it would appear feasible to determine rate of movement from a series of roentgenograms.

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SUBACUTE (PSEUDOTUBERCULOUS, GIANT CELL) THYROIDITIS AND ITS TREATMENT*

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THYROIDITIS is a relatively uncommon condition. In 1934 Cochrane and Nowak wrote, "It is no exaggeration to say that thyroiditis as an entity is unknown to the average internist and surgeon." Of the 251,072 new patients registered at the Cleveland Clinic from 1936 to 1947, a diagnosis of disease of the thyroid gland was made in 7,045. One hundred and forty-three had some type of thyroiditis and 93 had the subacute form which also sometimes is called pseudotuberculous or giant cell thyroiditis.

Apparently most reports in the literature on acute and subacute thyroiditis deal with inflammations due to bacterial infections. Table I lists several reports arranged according to the incidence of acute thyroiditis with and without suppuration.

TABLE I

Author	Year	Total Acute	Suppuration	Per Cent
Robertson	1911	96	40	42
Hagenbuch	1921	43	30	70
Burhans	1928	67	63	94
Cochrane and Nowak	1934	10	3	30
Means	1937	12	2	16
McQuillan	1938	17	6	35
Sallick	1942	12	1	8

In these reports the incidence of suppurative thyroiditis ranged from 8 to 94 per cent. In contrast to this, in our series of 143 cases of all types of thyroiditis, only 2, or less than 2 per cent, had suppuration. Bacterial thyroiditis is not the type under discussion. Suppuration does not occur in subacute thyroiditis and no organisms have been demonstrated in the tissues. The most common type of thyroiditis is a self-limiting disease, the etiology of which is unknown, though there are good reasons to suspect that viruses are responsible.

Dr. J. B. Hazard, Head of the Department of Pathology of the Cleveland Clinic, has suggested the classification for different types of thyroiditis as shown in Table II.

TABLE II

A. Specific Thyroiditis	
1. Bacterial	4
2. Parasitic	0
B. Nonspecific Thyroiditis	
1. Subacute (pseudotuberculous or giant cell)	93
2. Struma lymphomatosa (Hashimoto)	16
3. Struma fibrosa (Riedel)	11
4. Unclassified	19
Total cases	143

PATHOLOGY

The microscopic findings have been described by Hazard, as follows: The thyroid gland of subacute thyroiditis presents the following features: (1) fibrosis of variable degree, chiefly in the connective tissue partitions but also intralobular; (2) foci of small follicles with reduced or absent colloid; (3) infiltration of lymphocytes, polymorphonuclear leukocytes and plasma cells, foreign body giant cells and focal accumulations of histiocytes.

The connective tissue increase occurs as trabeculations of collagenous type of variable width and density, coinciding with anatomical partitions, and as a slight or moderate proliferation of interfollicular connective tissue separating and replacing

* From the Cleveland Clinic and the Frank E. Bunts Educational Institute. Presented at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.
† Former Fellow in Therapeutic Radiology, Cleveland Clinic.

acini. The follicles are reduced in number, small and formed by cuboidal epithelium. The lumina contain granular coagulum or a small amount of colloid frequently including collections of histiocytes. The general inflammatory infiltration is of moderate density most pronounced in the vicinity of follicles and is comprised principally of lymphocytes and polymorphonuclear neutrophils, with occasional plasma cells. Foreign body giant cells and foci of histiocytes may be frequent and usually coincide in location with follicular islands. The histiocytic foci at times contain rounded masses of colloid or may include a small collection of polymorphonuclear neutrophils. Caseous necrosis is never found. The foreign body giant cells may be large and not infrequently contain colloid masses.

CLINICAL FINDINGS

The clinical picture of subacute thyroiditis has been described by Crile and is quite typical. About one-third of our patients gave a history of recent mild upper respiratory disease. The principal complaints were pain in the neck or throat. It was quite characteristic for the pain to radiate to one or both ears. For these reasons some of our patients were examined first in the Department of Otolaryngology but no definite evidence of abnormality in the throat or ears attributable to or as a cause of thyroiditis was found. In addition to pain, patients complained of lassitude, increased fatigability, and nervousness. Weight loss, anorexia and dysphagia were common.

The onset of subacute thyroiditis in our cases was usually sudden. It nearly always developed in glands not previously noticeably enlarged but also in a few with preexisting goiters. The inflammation occasionally began in one lobe, then diffusely involved the whole gland which became swollen, firm, elastic, was movable and extremely tender, especially in early stages of disease. Regional lymph nodes were not enlarged by the inflammation. A low grade fever was usually present, seldom above 102° F. A few patients with severe reactions had chills followed temporarily by high fever. The pulse rate was often increased out of proportion to the temperature elevation. The sedimentation rate was usually elevated. In our series the basal metabolic rate ranged from minus 17 per cent to plus 30 per cent, the average being plus 10 per cent, and in only one-third was it over plus 15 per cent. White blood cell counts were normal. The whole clinical picture is one of a toxic reaction due to an inflammatory process in the thyroid gland.

All types of thyroiditis affect females predominantly. In this series only 10 per cent were males. The age incidence varied from twenty to sixty-three years, but most patients were between twenty-five and fifty-two years of age.

The natural course of the disease inclines toward spontaneous recovery without permanent damage to the gland. Some authors have stated that the condition usually subsides in a week or two. This, however, has not been our experience. Our patients presented themselves both early and late in the course of disease, many relating a history of the condition existing for two or more months. The extremes of duration were from two days to a year. Most patients remained well enough to carry on their ordinary activities although some were incapacitated by the systemic reactions and a few were so ill from extreme exhaustion, weakness, and toxicity that they were hospitalized and sent for roentgen therapy on litters.

TREATMENT

Some authors have advocated conservative treatment for subacute thyroiditis, and recommend rest, local applications of heat or cold, and administration of salicylates or thyroid extracts. We have observed no benefit from the use of sulfonamides or antibiotics. In 1945 King and Rosellini summarized a series of cases treated with thiouracil with benefit. Surgical operations are unnecessary for subacute thyroiditis. Biopsies may be made with the Silverman needle.

We began administering roentgen therapy for subacute thyroiditis in 1933. The technique has varied and is similar to that employed for other inflammatory processes. During the last few years the technique has been 200 kv., filter equivalent to 1.0 mm. half-value layer copper, 50 cm. distance and 100 or 150 roentgens skin dose every other day for four to six treatments. The size of portal may be 10 by 10 cm. or large enough to irradiate the entire gland.

Our colleagues in the Divisions of Medicine and Surgery agree that roentgen therapy is the best form of treatment. Crile wrote, "Subacute thyroiditis responds promptly and completely to roentgen ray therapy." Most patients were relieved of pain and tenderness after two or three treatments, the severity of other symptoms was reduced and the course of the disease shortened. Recurrence of symptoms in mild form developed in a few patients and were relieved by a second course of roentgen therapy. We have observed no deleterious effects from treatment; myxedema has not resulted, and the dosage is too small to cause skin reactions.

TABLE III

Cured with one course of roentgen therapy	40
Improved and second course followed by cure	6
Recurrences, no second course given	1
Untraced after treatment	8
Total cases	55

A possible explanation of the beneficial effects of roentgen therapy for subacute thyroiditis is supported by Lea's experiments proving that viruses are inactivated by radiation. We have shown similar beneficial effects with roentgen therapy for encephalitis attributed to virus disease.[17]

Of 93 of our cases having a diagnosis of subacute thyroiditis, 55 had roentgen therapy. The treatment was advised for 7 but we have no record of their having received it. They may have been treated elsewhere. Operation was performed on 14 and the diagnosis established by microscopic examination of tissues removed. Other methods of treatment were used for 17 cases. No information was obtainable about results in 8 cases. The results in cases given roentgen therapy are shown in Table III.

SUMMARY AND CONCLUSIONS

1. A series of 143 cases of thyroiditis seen at the Cleveland Clinic from 1936 through 1947 has been reviewed from the standpoints of incidence and classification.

2. The pathologic and clinical manifestations and diagnosis of subacute thyroiditis have been discussed.

3. The results of roentgen therapy for 55 cases of subacute thyroiditis have been presented.

4. Roentgen therapy is indicated and has been proved beneficial for subacute thyroiditis.

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DISCUSSION

Dr. Hugh F. Hare, Boston, Mass. I am pleased to hear this paper and to congratulate the authors on presenting us with the first group of patients with thyroiditis treated by irradiation. There have been a few sporadic reports but none revealing such large groups of cases. The course of the disease is limited and the patients tend to recover whether treatment is given or not. Certainly the relief of symptoms that they have obtained makes treatment more worthwhile and, too, they show that the course of the disease is shortened. Surgical intervention has been used, but not as satisfactorily, as reports show that myxedema occurs in 50 per cent of cases thus treated. Drs. Osmond and Portmann have really shown improved methods of handling these cases. I hope that they will go further than they have and try to differentiate the different types of thyroiditis.

SARCOMA OF THE UTERUS

A REPORT OF NINE CASES*

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SARCOMA of the uterus was first described clinically by Mayer in 1860 and one of his cases was confirmed pathologically by Virchow two years later.[9] Since that time there has been a voluminous literature which included several reports discussing the place of radiation therapy in the treatment of this condition. These reports are remarkable for the great differences in their evaluation of radiation therapy. The obvious reason for this difference of opinion is that it is extremely difficult to get a large enough series of patients so that a definite report can be written. There are also great variations in the methods of radiation therapy and of reporting results. As a consequence, it was decided to review the experience in the Radiation Therapy Department of Bellevue Hospital in an attempt to evaluate the effectiveness of radiation in the treatment of uterine sarcoma.

INCIDENCE

The incidence of sarcoma of the uterus is reported as varying from 0.5 per cent to 5.0 per cent of all malignant growths of the uterus.[7,10,14] Our series consists of 9 proved cases out of a total of 1,627 cases of malignancy of the cervix and corpus, an incidence of 0.56 per cent.

The range of ages as reported in the literature is extremely wide. The average seems to fall between the fifth and sixth decades. In our series the ages range from seventeen to sixty-eight years, with an average of 49.3 years. The average age of cases of carcinoma of the corpus in our series was 58.9 years.

In the series of cases reported in Veit's Handbuch[14] one-quarter of the patients were nulliparous and three-quarters parous. In our series 8 of the 9 cases were parous.

One of the most important problems discussed in the literature is the incidence of sarcomatous degeneration of fibroids. Many fibroids show marked cellularity and it is difficult to tell histopathologically when they are truly sarcomatous. The reported incidence varies from 0.4 per cent to 10.0 per cent. The figure most generally accepted is that 1 per cent of all myomas show sarcomatous degeneration.[5] Obviously this difference in diagnostic criteria causes a great variation in the reported results.

Corscaden and Stout[4] found that, despite the many thousands of cases of fibroids of the uterus treated with irradiation, only 4 cases of sarcoma were reported as occurring in this group. They concluded that the only safe criteria for the diagnosis of sarcoma arising in a fibroid is infiltrative and destructive growth, rather than microscopic criteria. We believe that this is a good approach to a difficult problem.

DIAGNOSIS

The symptoms do not differentiate this condition from fibroid tumors or carcinomas. The cardinal symptoms in all are hemorrhage, discharge, and pain. Pain and debility may occur relatively earlier in sarcoma than in carcinoma because of the more rapid rate of growth and concurrent necrosis. However, Smith[13] found pain to be a symptom in only two-fifths of his patients.

The physical findings are also not characteristic.

As a result, the diagnosis will rest on pathological examination. The specimens

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may be obtained by dilatation and curettage, or after hysterectomy. Most authors state that the diagnosis is usually not made until after hysterectomy. Therefore their reports do not consider preoperative irradiation as a method of treatment applicable to the problem. However, a certain percentage of sarcomas are present in the uterine cavity and are diagnosed by curettage. Wolfe[16] states that this occurred in 50 per cent of his cases. In our series the pathological diagnosis was made before hysterectomy in 4 of the 9 cases.

PATHOLOGY

Ewing[6] has divided this group of tumors into mural and mucosal sarcoma. However, in advanced cases it may be almost impossible to tell where the sarcoma arose.

In any case the cell type may have a prognostic significance. Ewing's classification included: (a) recurrent myoma; (b) spindle cell; (c) round cell.

The most benign is the relatively rare recurrent myoma which has an orderly arrangement of cells with well formed vessels.

The next most malignant group are those with spindle cells. They have granular cytoplasm, vesicular nuclei, and occasional giant cells. They invade the parametrium, broad ligaments and mucosa with ulceration, necrosis, and cachexia.

Those sarcomas which are composed primarily of round cells are even more malignant. They grow rapidly, and quickly produce local destruction, cachexia and metastases.

Novak and Anderson[10] added a mixed cell group which is more malignant than those previously mentioned.

Ewing believed the entire group to be of myogenic origin. However, he stated that there is evidence that endometrial sarcomas may arise from stroma cells.

Carcinosarcoma is another type that has been discussed in many reports. It is still an ill-defined entity. Ewing believed that many of the cases reported were due to atypical growth of the epithelial cells or atypical reactions of the stroma, since the metastases were usually shown to be carcinomatous. Case IX in our series illustrates the difficulty of making this diagnosis.

Gessner[14] found distant metastases in 24 of 33 autopsied cases. These included metastases to the lungs in 15 cases, to the liver in 10 cases, to the intestine in 8, to the omentum in 5, to the kidney in 5, to the pleura in 5, and a smaller number in other organs.

Brooke and Thomason[3] found only four reports in the literature of bone metastases which were demonstrated on roentgenograms. Case VIII in this series had a metastasis to the skull (Fig. 1).

FIG. 1. Case VIII. Roentgenogram of skull showing area of metastasis. This region has been overexposed to show the bony spicules and soft tissue detail.

REVIEW OF METHODS OF TREATMENT AND PROGNOSIS

The reports in the literature are not strictly comparable because of the varied criteria for malignancy in fibroids. As a consequence, no attempt has been made to present an exhaustive review of the literature. Some of the outstanding articles have been abstracted to illustrate the confusion that exists about the value of radiation therapy in the treatment of sarcoma of the uterus.

Every article is in complete agreement that the primary means of treating this condition is early, complete surgery. Never-

theless there are several reports of cases treated by irradiation alone.

Seitz and Wintz[12] in their report found that 4 of 8 inoperable cases treated with roentgen therapy were well for three years without evidence of recurrence. Béclère[1] culled 9 cases from the literature which were treated by irradiation and were without recurrence from two to seven years after treatment. Both of these reports were quite enthusiastic as to the effectiveness of irradiation.

On the other hand, Regaud and Lacassagne[11] treated 6 inoperable cases by irradiation. They found that 5 of these died within six months and only one was well for three and a half years. As a result, they felt that irradiation alone was of little value in the treatment of uterine sarcoma.

Masson[8] reported that 72 per cent of cases with sarcoma in a fibroid survived three years after operation.

Bosse and Stanton[2] found that none of their 13 cases with evidence of invasion survived five years despite radiation therapy, while 12 of their 14 cases without evidence of invasion were well for five years.

Smith[13] found that none of his 24 patients survived more than four years. He felt that irradiation had no effect whatever on the course of the disease.

Kimbrough,[7] in his excellent statistical study of 43 cases, reported a total five year survival rate of 34.3 per cent for 35 of his cases. The operative mortality in his series was 4 out of 36 patients. Only a few of his cases received radiation therapy. However, he reported one case that was treated for recurrence and was well for six years after radiation therapy.

Novak and Anderson[10] prefer a panhysterectomy followed by irradiation. They reported 15 of their 50 cases well after five years, with 3 additional deaths before ten years. The operative mortality in their series was 7 out of 50 cases.

Von Kovesligethy[15] reported 32 cases in which panhysterectomy was done in 20 followed by radiation therapy. Five of these survived five years. Two of the 12 patients treated with irradiation alone survived five years. He felt that those cases which did not survive five years showed good palliative results.

We feel that preoperative radiation therapy should be used in all cases diagnosed by curettage. This should preferably be in the form of intrauterine radium, and should be followed by panhysterectomy in six to eight weeks. All cases, whether treated preoperatively or not, should have intensive postoperative deep roentgen therapy. In advanced cases, palliative radiation therapy should be administered.

REPORT OF CASES

Group A. Cases in which combined surgery and irradiation were used.

CASE I. C. M., a colored housewife, aged fifty-eight, was admitted in July, 1931, with a chief complaint of vaginal bleeding and intermittent lower abdominal pain for four months. Menstruation started at fourteen years and occurred every thirty days for four days' duration. Menopause occurred at the age of forty-five. She was gravida IV, para III, with one uncomplicated instrumental abortion at two and one-half months.

The diagnosis on admission was fibromyoma of the uterus, and a supracervical hysterectomy was performed.

Pathological study of the removed organs showed the wall of the uterus to be 2 cm. thick, smooth and streaked yellowish red. A large, yellowish red, irregular mass of tissue projected into the lumen from the posterior wall of the endometrial cavity. This completely filled the cavity. This tissue was very friable and revealed soft, yellowish white, and in spots hemorrhagic core on section. Microscopic diagnosis was mixed spindle and round cell sarcoma.

Treatment and Course. Postoperative roentgen therapy of 100 per cent skin erythema dose was given to four 10 by 15 cm. pelvic fields. (This was the unit of dosage in use at that time.) The factors were: 200 kv., 5 ma., with 0.5 mm. Cu plus 0.9 mm. Al filter, at 80 cm. distance. Half-value layer 0.9 mm. Cu.

The results in this patient were not ascertained because she did not return for further treatment or follow-up.

CASE II. L. M., a white female, unmarried, aged seventeen, was admitted to our service in

November, 1935, with a chief complaint of pain in the left lower quadrant for one month. Menstruation started at fourteen years and occurred every twenty-eight days for four days' duration. She had never been pregnant.

Physical examination on admission revealed the cervix to be posterior and the uterus forward, firm, and enlarged to 2 cm. above the symphysis. It was quite movable and no adnexal thickening was palpable.

Dilatation and curettage showed an irregular cavity with bits of necrotic tissue, but a pathological diagnosis was not made. Following this a supracervical hysterectomy was done.

Pathological examination showed the uterus to be 6 by 10 by 10 cm. in size. The surface was covered by smooth pink serosa except for an area on the right superior anterior aspect at which place there was a soft, shaggy, friable mass projecting through the serosa through an opening 6 cm. in diameter. On each lateral aspect of this there was a subserous swelling measuring 3 by 4 cm. Filling the uterine cavity was a ragged necrotic mass which measured 3 by 6 cm., the tissue of which resembled that projecting through the anterior wall.

Microscopically the greater part of the tissue was pale blue cells which infiltrated the stroma in all directions. The cells had fairly large pale blue vesicular nuclei with a relatively small amount of cytoplasm with indistinct cell outlines. Many mitotic figures were seen. The diagnosis was sarcoma of the uterus.

Treatment and Course. The patient was given 750 r (measured in air) over two 10 by 15 cm. anterior pelvic fields and 600 r (air) over two 10 by 15 cm. posterior pelvic fields. The small amount of therapy was due to the patient's refusal to continue treatment. After six months, however, she returned to the clinic at which time she was given an additional 450 r (air) over each of the four areas. The factors were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at a distance of 40 cm. Half-value layer 0.9 mm. Cu.

This patient has been followed up to the present time (1948) and is without complaint or evidence of recurrence. The total survival time is thirteen years.

Case III. M. S., a white female, married, aged forty-six, was admitted to our service in July, 1937, with a chief complaint of vaginal bleeding for three years. This took the form of gradually increasing menstrual periods. She had been operated upon one year before at another hospital and was told that she had tumors of the uterus but not all of them were removed. She continued to have menstrual as well as intermenstrual bleeding after that operation. Menstruation started at seventeen years and occurred every twenty-eight days for seven days' duration. She was gravida VII, para VI with one spontaneous abortion at four months.

Physical examination showed the fundus to be irregular and enlarged half way to the umbilicus. The cervix, parametria and adnexa were apparently normal. Her hemoglobin was 3.5 gm. and red blood cell count 1,500,000.

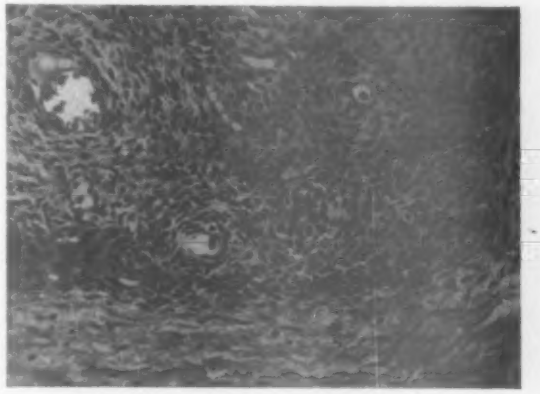

Fig. 2. Case III. Well differentiated sarcoma of uterus.

After several transfusions a supracervical hysterectomy, bilateral salpingo-oophorectomy, and excision of the right infundibulopelvic ligament was performed. This ligament was excised because there was gross evidence of tumor invasion.

Pathological examination showed the uterus to be enlarged to three times normal size and to be nodular. Some of these nodules were due to intramural fibroids. Extending through the right side of the uterus was a soft neoplastic growth which appeared to be malignant tissue and which extended into the blood vessels of the broad ligament and right infundibulopelvic ligament. The tumor was cut across at the right broad ligament. Histopathologically the cells were not very malignant but extension into the extrauterine tissue was unquestionable (Fig. 2).

The diagnosis was sarcoma of the uterus, arising from endometrial stroma, cut across at the broad ligament.

Treatment and Course. Postoperatively the patient was given 1,500 r (air) to each of two 20 by 20 cm. anterior pelvic fields; 1,800 r (air) to

each of two 20 by 20 cm. posterior pelvic fields; and 1,350 r (air) to each of two 20 by 20 cm. lateral pelvic fields. The factors used were: 200 kv., 20 ma., with 0.5 mm. Cu. plus 1.0 mm. Al filter, at 50 cm. distance. Half-value layer 0.9 mm. Cu. The estimated tumor dose was 2,250 r in a period of forty-five elapsed days.

She was followed without evidence of recurrence until September, 1941, when she moved to another city and was lost to follow-up. This patient was well for the four years and two months she was followed in the radiation therapy clinic.

This case illustrates the importance of postoperative irradiation. There was a long survival despite the fact that not all the tumor tissue was removed by surgery.

CASE IV. C. G., a white widow, aged forty-nine, was admitted to the gynecological service in April, 1945, with a chief complaint of intermenstrual bleeding for two weeks before admission associated with a steady severe pain in the left lower quadrant. Menstruation started at thirteen years and occurred every twenty-eight days for five days' duration. She was gravida IV, para IV.

On admission, physical examination revealed a parous introitus. The cervix was dilated two fingers. The fundus as such was not outlined but was incorporated in a firm irregular mass the size of a four to five month gestation. The mobility of this mass was limited. The adnexa and parametria were free. Speculum examination showed the cervix to be patent and a foul necrotic mass was seen protruding from the external os.

The patient had a supracervical hysterectomy and bilateral salpingo-oophorectomy for supposed fibromyomas of the uterus.

Pathological examination showed that the uterus measured 12.5 by 10 by 7 cm. The surface was smooth but the contour was irregular due to the presence of a large intramural fibroid, measuring 7 cm. in diameter. On section it had a yellowish appearance and the consistency was rubbery. Several other intramural fibroids were present varying in size. The endometrial cavity was greatly distorted by a large pedunculated submucous fibroid 8 cm. long and 5 cm. in diameter.

Microscopically sections through the submucous fibroid showed hyalinization, necrosis, liquefaction, and calcification. Sections through the waxy intramural fibroid showed great variability of cells with anaplasia, mitosis, and invasion into blood sinuses.

The pathological diagnosis was sarcoma of the uterus.

Treatment and Course. Roentgen therapy consisting of 2,000 r (air) to four 20 by 20 cm. pelvic fields was administered in thirty-five elapsed days. The factors were: 200 kv., 20 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 50 cm. distance. Half-value layer 0.9 mm. Cu. The estimated tumor dose was 2,500 r to each parametrium.

The patient has been followed without complaint or evidence of recurrence until the present time (1949). The time followed to date is three and one-half years.

CASE V. A. W., a widowed colored woman, aged thirty-four, was admitted to the gynecological service in October, 1947, with a chief complaint of low back pain for seven months and swelling of the abdomen for three months. She had a 35 pound weight loss over this period. Menstruation started at fourteen years and occurred every thirty days for three days' duration. She was gravida III, para II, with one spontaneous abortion at five months.

Physical examination on admission revealed a symmetrical firm abdominal mass arising from the pelvis which was palpable to a point 1 cm. above the umbilicus. The cervix was firm, posterior and closed. There was no bleeding from the cervix although it was apparently attached to the mass above. No separate masses were palpable.

Roentgenography revealed small and large nodular infiltrations of both lungs. The findings were those of metastasis (Fig. 3).

Exploratory laparotomy was done with a diagnosis of ovarian carcinoma. A large tumor mass was found attached to the uterus, left ovary and omentum. Complete removal was impossible, but the greater part of the lesion was removed.

Pathological examination showed that the specimen was a supravaginal portion of the uterus incorporated in an irregular lobulated 25 by 23 by 22 cm. mass. The endometrial cavity was filled with necrotic brown material apparently arising from the endometrium. The wall of the uterus was broken through in several places and in direct communication with large irregular tumor lobules which arose from all sides of the corpus. The surface of the tumor showed no definite capsule.

Microscopically the endometrium and portion of the myometrium were completely replaced by highly undifferentiated anaplastic

cells. These were in general of the spindle cell type. However, there were round cells in all areas. The nuclei showed marked hyperchromatism and variation in size and shape. Mitoses were numerous.

The pathological diagnosis was sarcoma of undetermined type, probably leiomyosarcoma of the uterus.

The patient had a very stormy postoperative course. When she recovered her only complaints were severe pain in her chest and moderate cough.

Roentgen examination again revealed the nodular infiltration of both lungs.

At this time she was given a course of 5 mg. of nitrogen mustard intravenously over a four day period. This had no effect on the size of the metastases or the severity of her symptoms.

Fig. 3. Case v. Roentgenogram of chest showing nodular densities in both lung fields.

Following this the patient was treated with roentgen therapy and was given 1,800 r (air) to an anterior and a posterior 10 by 15 cm. right mediastinal field. The factors were: 200 kv., 20 ma., with a Thoraeus filter, at 50 cm. distance. Half-value layer 2.0 mm. Cu. The estimated tumor dose was 1,430 r to the mediastinum in sixteen days. After this course the patient's pain completely disappeared, although her cough was only slightly improved. Roentgenograms showed no change in the size of the lesions in the chest. This represents an excellent palliative response to roentgen therapy after nitrogen mustard therapy had proved ineffective.

Group B. Inoperable cases which were treated by irradiation alone.

Case vi. F. M., a housewife, married, aged sixty-five, was admitted to our service in September, 1925, with a chief complaint of severe pain in the lower abdomen and vaginal bleeding for three days before admission. Menopause occurred at the age of forty-eight. She was gravida 1, para 1. No further menstrual history is available.

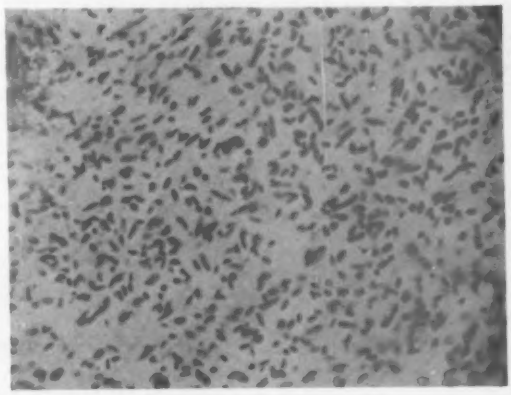

Fig. 4. Case vi. Spindle cell sarcoma.

On admission the cervix was soft, irregular, and patulous. Uterus and adnexa were not palpable. Speculum examination revealed a bloody discharge coming from the cervix.

Dilatation and curettage was done and the pathological report was spindle cell sarcoma with an occasional giant cell (Fig. 4).

Treatment and Course. Operation was contraindicated by the age and general condition of the patient. She was treated only with radiation therapy.

In August, 1925, a tandem of four tubes of radon filtered with 1 mm. platinum was inserted into the uterus for a total of 3,724 millicurie-hours. This was followed by roentgen therapy of 50 per cent skin erythema dose to anterior right and left 10 by 15 cm. pelvic fields, and 75 per cent skin erythema dose to posterior right and left 10 by 15 cm. fields. (The skin erythema dose was the unit in use at that time.) The factors used were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

She was well until June, 1927, when she had a recurrence of bleeding for two days. She was treated with a radium tandem as before for an additional dosage of 3,132 mc-hr.

The patient was well until January, 1928,

when she began to bleed from the cervix again. Curettage at this time revealed sarcoma. Another radium tandem was inserted for a dosage of 2,879 mc-hr.

The patient was followed without complaint until March, 1928. At that time she did not return to the clinic. The time followed was two and a half years. This illustrates a good palliative result from radiation therapy alone.

CASE VII. S. B., a housewife, aged sixty, admitted in June, 1933, with a chief complaint of vaginal bleeding for five months. She was bedridden from the anemia as well as her rheumatoid arthritis. Menstruation started at fourteen years and occurred every twenty-eight days for four days' duration. Menopause occurred at age of fifty. She was gravida V, para III, with two spontaneous abortions at five and five and one-half months.

Physical examination showed that the patient had severe generalized rheumatoid arthritis and severe anemia.

Gynecological examination revealed a two finger introitus with a relaxed pelvic floor. There was a moderate cystocele and rectocele. The cervix was shortened and patulous. It admitted the tips of two fingers. The fundus was not palpable because of a tense abdomen but the adnexa appeared to be free. On speculum examination the rim of the cervix was easily pushed apart and large meaty clots of blood and tissue were easily removed from the cervical canal.

The pathological report of these clots was spindle cell sarcoma.

Treatment and Course. Because of her poor general condition this patient was treated by irradiation alone. She was given 800 r (air) to each of two 10 by 15 cm. anterior pelvic fields and 1,000 r (air) to each of two 10 by 15 cm. posterior pelvic fields. The factors were: 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

Following this a sound containing three tubes of 15 mg. radium each filtered with 1.5 mm. platinum and a colpostat and cork with a 10 mg radium tube filtered with 2.5 mm. platinum in each cork were inserted into the uterus and vagina. The total dosage was 4,320 milligram-hours in the uterus and 1,920 mg-hr. in the vagina.

One month later she was given another course of roentgen therapy of 1,200 r (air) to four 10 by 15 cm. pelvic fields. She was also given 2,000 r (air) to both suprapubic and sacral areas, of 10 by 15 cm. each. Factors used were 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, 40 cm. distance. Half-value layer 0.9 mm. Cu.

The patient improved markedly and was up and about. Her fundus remained two fingers above the symphysis and a slight serosanguineous discharge persisted. In April, 1934, she moved to another city and was lost to follow-up. Time followed was ten months. This patient had a good palliative effect despite her poor initial condition.

CASE VIII. B. M., a housewife, aged fifty-eight, was admitted in October, 1933, with a chief complaint of vaginal bleeding for ten months. Nine months before a diagnosis of sarcoma had been made and she was treated with intrauterine radium at another hospital (amount unknown). Bleeding continued and the patient developed lower abdominal pain. At this time she was admitted to our service. Menopause occurred at forty-six. She was gravida XVIII, para XIII. Further gynecological history was not obtained.

Physical examination showed a chronically ill patient. The cervix was clean and the uterus retroflexed. There was tenderness and fullness in both fornices. The rectum was so narrowed and tender that rectal examination was impossible.

Treatment and Course. A dilatation and curettage was done. Following this a sound containing three tubes of 15 mg. each of radium filtered with 1.5 mm. platinum was inserted into the uterus for a dosage of 6,345 mg-hr.

Pathological diagnosis of the curettings was mixed spindle and round cell sarcoma.

She improved only slightly and two months later developed severe headaches. Examination revealed a mass attached to the skull. Roentgenogram showed an osteoblastic osseous change about 2 cm. across, situated 5 cm. posterior to the bregma. The bony deposit was perpendicular to the external table (Fig. 1).

This area in the skull was treated with 25,000 mg-hr. with the 5 gram radium pack at a distance of 6 cm., with a filtration of 5.0 mm. lead and 0.5 mm. platinum. This was followed by 1,200 r (air) to each of four 10 by 15 cm. pelvic fields and 2,000 r (air) over the skull lesion. The factors were 200 kv., 4 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 40 cm. distance. Half-value layer 0.9 mm. Cu.

There was no improvement. The patient's course was retrogressive following therapy and she died in September, 1934.

Autopsy revealed a sarcoma arising in a

uterine fibroid with pulmonary and pleural metastases. There were also metastases to the liver, mesentery, ovaries and ribs.

Total time followed with disease was one year and five months.

This patient had little relief from radium or roentgen therapy.

This is the fifth case reported in the literature with bone metastases from a uterine sarcoma demonstrated on roentgenograms.*

Case ix. M. T., a housewife, aged sixty-one, was admitted to our service in October, 1937, with a chief complaint of spotting of bright red blood for fifteen months. For four months this had been accompanied by a sharp pain in the right lower quadrant. Menstruation began at thirteen years and occurred every thirty days for seven days' duration. Menopause occurred at the age of forty-five. She was gravida vii, para vii.

Physical examination revealed an acutely and chronically ill patient. The abdomen was tense and a fluid wave was present. The cervix was atrophic and the parametria soft. The uterus was not palpable. Rectal examination revealed a large, firm, cystic mass in the cul-de-sac. This was about 10 to 15 cm. in diameter and seemed to originate in the left adnexa.

A curettage was performed and pathological examination of the curettings revealed a compact arrangement of strands, cords, and nests of an epithelial type of cell growing in a totally irregular fashion in a fibrous tissue stroma. Cells were large with poorly defined outlines, but with an abundant cystoplasm. Nuclei were large, varied in size and shape, and were pale staining. Distinct mitoses were seen in the majority of nuclei. In other areas the cells were of a spindle cell type, with smaller deeply staining nuclei, and retaining their compact cellular arrangement (Fig. 5 and 6).

The pathological diagnosis was transitional cell epithelioma showing in several places highly suspicious signs of a genuine spindle cell sarcoma.

Treatment and Course. The patient was very weak and received only 750 r (air) to each single 20 by 20 cm. anterior and posterior pelvic field. The factors were 200 kv., 5 ma., with 0.5 mm. Cu plus 1.0 mm. Al filter, at 80 cm. distance. Half-value layer 0.9 mm. Cu.

On completion of therapy the patient signed out of the hospital and did not return.

* Since this report we have had another case with a mixed osteoplastic and osteolytic metastasis to a lumbar vertebra.

This is presented as a possible case of carcinosarcoma.

COMMENT

These 9 cases include 2 in which apparently complete removal of the tumor was

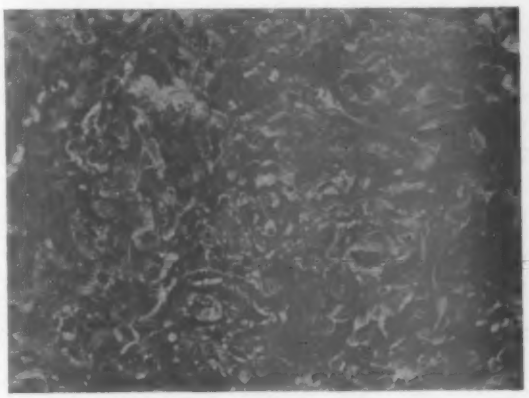

Fig. 5 Case ix. Section showing highly anaplastic carcinoma

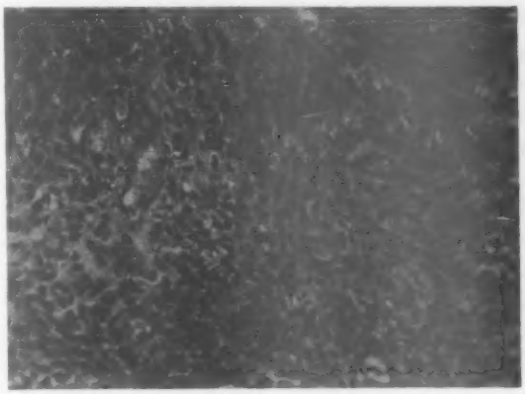

Fig. 6. Case ix. Section of same specimen showing an area strongly suggestive of sarcoma.

followed by deep roentgen therapy, and who survived without recurrence thirteen years and three and one-half years respectively.

One patient had incomplete removal of the tumor followed by intensive irradiation. She was followed without evidence of recurrence for four years and two months after therapy.

Three of the 6 advanced cases showed marked palliative effect and only one showed little response to radiation therapy.

Two cases were lost during the course of therapy and no evaluation of their response can be made.

Examination of all these cases has convinced us that radiation therapy is very important adjuvant in the treatment of these patients.

We feel that there is a very definite place for preoperative roentgen or radium therapy since many of the patients are diagnosed by dilatation and curettage before hysterectomy. This is certainly true in view of the high operative mortality reported in several series.[7,10] The debilitating effect of this rapidly necrosing tumor undoubtedly contributes to this mortality. Intrauterine radium would do much to improve the preoperative condition of those patients whose tumors are present in the uterine cavity. Preoperative roentgen therapy may be used for the same purpose if the uterine cavity is so filled with neoplasm that insertion of radium is impossible. Cases VI and VII illustrate the remarkable improvement in general condition that followed radiation therapy. Total hysterectomy should follow irradiation in six to eight weeks.

Postoperative high voltage radiation therapy is indicated in all cases. Small foci of neoplasm can easily be left behind despite apparently adequate surgery. We feel that irradiation will arrest these foci in some cases. There are several cases in the literature which were followed over long periods of time despite residua or recurrence after surgery. Case III is another example of this.

Radium and roentgen therapy have a definite place as a palliative measure in advanced cases. Several of this series of cases showed gratifying palliation with radiation therapy.

SUMMARY

Nine cases of sarcoma of the uterus are presented and their treatment discussed.

Three operable cases were treated by combined surgery and postoperative roentgen therapy. Two are still well thirteen and three and a half years respectively. One was followed for four years and two months without recurrence even though tumor was known to be left by surgery.

Six inoperable cases were treated by irradiation alone. Three of these had comfortable life prolonged by radiation therapy.

I wish to express my appreciation to Dr. Rieva Rosh, Visiting Radiation Therapist at Bellevue Hospital, for her help and encouragement in the preparation of this report.

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STUDIES ON THE METABOLISM OF RADIOISOTOPES BY VARIOUS FUNGI AND BACTERIA

THE DISTRIBUTION OF ORGANISMS CONTAINING RADIOIODINE (I^{131}) IN THE ANIMAL BODY

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RADIOACTIVE iodine (I^{131}) has been used for some time in the study of thyroid physiology, and its distribution in tissues in relation to time of administration is well known.[1,3,7,9,10,15,16,23,24,25,27] It is known that certain thyroid carcinomas alter the iodine distribution.[5,8] This paper will deal with the apparently altered distribution of I^{131} when the solutions administered consist of spores or bacteria which have been grown in the presence of radioactive substance. The technique for raising "radioactive" fungi has been previously reported[21] but since then it has been rechecked and increased in scope.

MATERIALS AND METHODS

The radioactive I^{131} was received from the Atomic Energy Commission and was standardized immediately prior to use. A calculated dose was administered and in each experiment all of the radioactivity was finally accounted for.

The fungus cultures used in this study were from the stock culture supply of the Department of Bacteriology and were grown on Sabouraud's agar slants.

The cultures were checked grossly and also microscopically for spores and each culture tube was filled to the top of the agar slant with either sterile distilled water or physiological saline. These cultures were then taken to the isotope laboratory where the radioactive isotope was added to the clear solution (I^{131} 20–1,000 microcuries). During this transfer of radioactive iodine, two persons were involved and both used protective aprons and gloves. One person pipetted the calculated dose of I^{131} with proper equipment, while the other person handled the cultures with tongs. All equipment and personnel involved were checked for radioactive contamination upon completion of the transfers. The cultures were exposed to these solutions for forty-eight to 120 hours in the isotope laboratory.

After exposure, the cultures were taken to the bacteriology laboratory to be filtered. Here the cultures, Seitz filters to be used, and suction flasks were placed on a metal tray behind a protective shield, and all transfers and manipulations were made over the shield to prevent contaminating the laboratory with radioactive material or exposing the personnel. The person doing the filtering wore rubber gloves and apron and handled the test tubes with 12 inch tongs. Each culture was washed with sterile saline (three to five washings) until the filtrate was essentially radionegative. Each washing was collected in a 15 cc. centrifuge tube placed inside the suction flask and a Geiger count done on it. This tube also prevented contamination of the vacuum equipment by the radioactive solution.

When the filtrate was essentially radionegative, the material left upon the Seitz filter was tested for radioactivity; if positive, it was resuspended in saline and examined with a microscope to insure the presence of spores and mycelia. If this suspension was considered satisfactory, it was drawn into a sterile lead-protected 10 cc. syringe and injected intravenously into animals. Geiger counts were done on these animals thirty minutes after injection and daily thereafter.

Small amounts of the fungi remaining on the Seitz filter were smeared on microscope slides and checked with the Geiger counter for radioactivity. If considered sufficiently active to make a radioautograph, the slides were taken to a dark room and placed in contact with photographic plates for variable times, depending upon the amount of radioactivity (two to fourteen days).[5] An extremely fine grain photographic emulsion is necessary to record these small organisms. Kodak Nuclear Track plates,

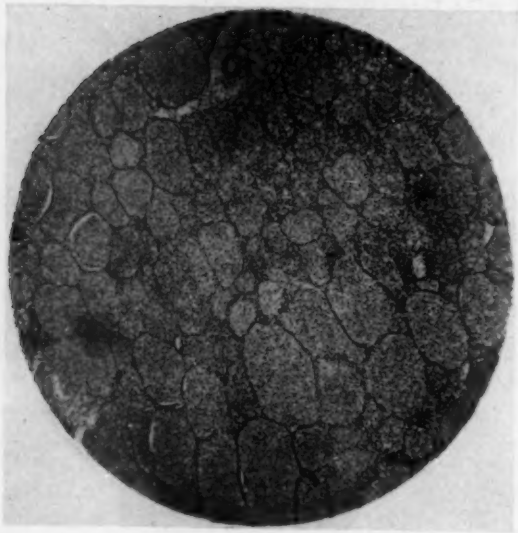

FIG. 1. Radioautograph of thyroid of a normal dog forty-eight hours after administration of 500 microcuries of I^{131} intravenously, showing the iodine distributed throughout the cells and colloid in a uniform manner. ×200. Hematoxylin and eosin stain on radioautograph.

Type NTB (25 Micron) were used.* These plates were then developed and the corresponding slide stained and both were examined microscopically.

* The authors wish to thank the Eastman Kodak Company who supplied the plates.

Pathogens (*Mycobacterium tuberculosis*, etc.) were handled essentially this way, except that the slide and film were kept in a petri dish which could be sterilized after completion of the radioautographs. As previously described, the pathogenic spore formers were always handled under a layer of liquid to prevent the dissemination of spores or radioactive particles into the air. The plates were developed in beakers which could also be sterilized after use.

RESULTS

Figure 1 shows a radioautograph of the thyroid of a normal dog made from animal 47–264. This animal received 500 microcuries of I^{131} intravenously forty-eight hours prior to a hemithyroidectomy. The technique used in preparing this specimen was that of Evans.[5]

Table 1 indicates by + signs the relative distribution of I^{131} in the various organs at the times that the animal was checked for radioactivity.

(1) It can be seen that, when various organisms have been exposed to I^{131} (animals 5–13), the iodine does not go directly to the thyroid gland as in the case of inorganic I^{131} solution (animals 1–4).

(2) If organisms are administered intravenously to the dog prior to exposure to

TABLE I

TABLE SHOWING THE RELATIVE DISTRIBUTION OF RADIOACTIVE IODINE FOLLOWING THE ADMINISTRATION OF STERILE INORGANIC I^{131} SOLUTION AND SUSPENSIONS OF MICRO-ORGANISMS WHICH HAVE BEEN MADE RADIOACTIVE

Dog No.		1*	2	3	4	5	6	7	8	9	10	11	12	13	14
1. (8–85) 16 lb. female brown chow, 100 microcuries I^{131}	T.**	1+	4+	4+	4+	3+	3+	2+							
	L.	3+	3+	1+	1+	1+	1+	±							
	S.	4+	3+	2+	1+	1+	1+	±							
	B.		±	±	±	o	o	o							
2. (47–264) 20 lb. female white mongrel, 500 microcuries I^{131}	T.		4+	4+											
	L.		2+	1+											
	S.		2+	1+											
	B.	4+	±	±											
3. (47–265) 19 lb. female brown mongrel, 1,000 microcuries I^{131}	T.		4+	4+											
	L.		2+	1+											
	S.		2+	1+											
	B.	4+	±	±											
4. (47–239) 20 lb. male black mongrel, 500 microcuries I^{131}	T.		4+	4+											
	L.		1+	1+											
	S.		1+	1+											
	B.	4+	±	±											

TABLE I—(*continued*)

Dog No.		1*	2	3	4	5	6	7	8	9	10	11	12	13	14
5. (47–78) 38 lb. female mongrel, *Alternaria* spores and I^{131}	T.	1+		1+			1+				1+				3+
	L.	3+		3+			2+				1+				o
	S.	3+		3+			3+				2+				o
	B.	1+		2+			1+				1+				o
6. (47–264, 48–5) 20 lb. male, white, long-haired, *Fusarium* and 20 microcuries I^{131}	T.	1+		3+							2+				
	L.	3+		1+							1+				
	S.	3+		o							1+				
	B.	1+		o							1+				
7. (48–5, 47–264) 18 lb. male, white, *Alternaria* and I^{131}	T.	3+	2+	2+	1+	1+	o	o							
	L.	4+	3+	4+	1+	±	o	o							
	S.	4+	2+	3+	1+	±	o	o							
	B.	2+	2+	1+	1+	±	o	o							
8. (48–85) 16 lb. female brown chow, *Alternaria* and I^{131}	T.	1+	1+	1+	±	±	±	2+	1+	o					
	L.	3+	3+	1+	3+	3+	3+	2+	±	o					
	S.	3+	1+	2+	3+	3+	3+	2+	1+	o					
	B.	1+	1+	1+	±	±	±	2+	1+	o					
9. (48–65) 15 lb. male bull, *Fusarium* and I^{131} (shock from *Fusarium*)	T.	o													
	L.	o													
	S.	o	o												
	B.														
10. (47–251) 20 lb. female brown chow, *Oospora* and I^{131}	T.	2+	1+	1+	±	1+	1+	o							
	L.	2+	1+	1+	o	o	o	o							
	S.	3+	1+	1+	o	1+	1+	o							
	B.	1+	1+	1+	o	o	o	o							
11. (47–147) 24 lb. female, black and brown terrier *Blastomyces*, *Actinomyces*, *Monilia*, *Histoplasma*, *Cryptococcus*, *Sporotrichium* and I^{131}	T.	1+		1+					1+						o
	L.	2+		2+					1+						o
	S.	2+		2+					2+						o
	B.	1+		1+					1+						o
12. (47–243) 30 lb. male, black hound, tubercle bacilli and I^{131}	T.	2+	2+	3+	1+	±	o	o							
	L.	1+	1+	1+	1+	1+	±	±							
	S.	1+	1+	1+	o	o	o	o							
	B.	1+	1+	1+	o	o	o	o							
13. (47–251) 20 lb. female brown chow, *Fusarium* intravenously, I^{131} intravenously, 20 microcuries	T.	4+			4+							4+			
	L.	2+			o							±			
	S.	2+			1+							±			
	B.	1+			o							±			
14. (00–000) 15 lb. male, black and white, *Fusarium* and 50 microcuries I^{131}	T.	2+	3+	4+											
	L.	3+	1+	—											
	S.	2+	1+	—											
	B.	2+	1+	—											

* 30–60 minutes.
** Thyroid, Liver, Spleen, Bladder.
± = doubtful.

I^{131} (animals 13–14) and inorganic I^{131} solution administered later, the iodine is distributed in the same manner as in the controls (1–4).

Animal 48–85 (8) was given *Alternaria* + I^{131} and the iodine did not go to the thyroid directly. Several months later the same animal was given 100 microcuries I^{131} (1) which followed the expected iodine distribution.

Figures 2, 3 and 4 show radioautographs of microorganisms (see explanation of plates).

DISCUSSION

As we have shown in a previous publication,[21] all of the radioactive element present

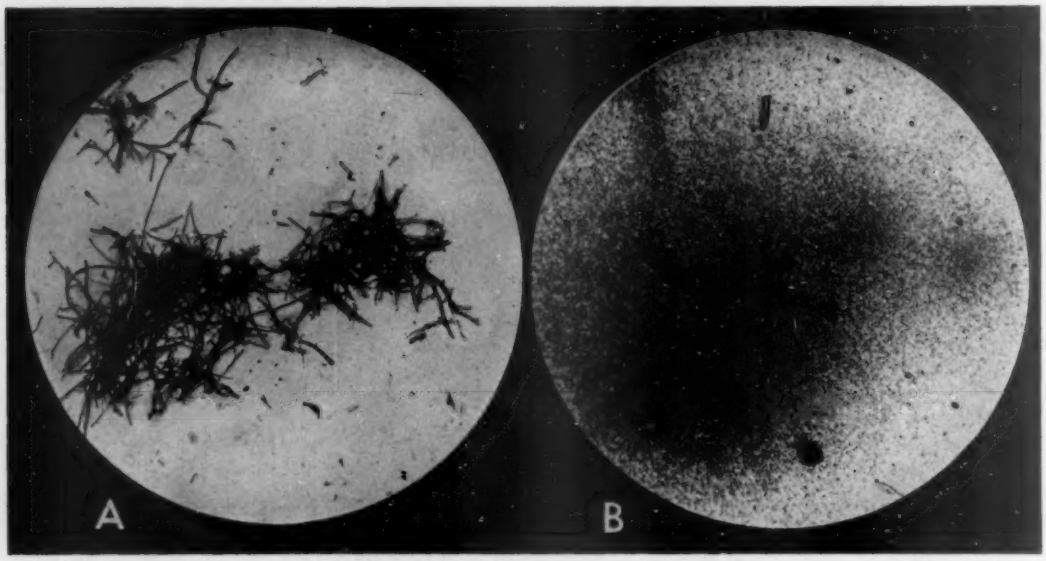

FIG. 2. *A*, *Fusarium* after a ninety-six hour exposure to 300 microcuries of I^{131}. Dilute methylene blue stain. ×200. *B*, radioautograph of *A*.

in the suspensions of organisms which were injected into animals had been actually metabolized by and incorporated into the organisms. The concentrations of pure organisms on the filters were leached and washed until the washings gave less than 10 counts per minute per milliliter above background. The organisms were then resuspended in fresh (non-radioactive) sterile saline. In subsequent radioautographs, the organisms proved to be very active, while neither the dried suspension medium nor fibers from the Seitz filters showed any detectable activity.

Animals 1–4 are the control animals that received dosages of 100 to 1,000 microcuries of I^{131} intravenously. These animals revealed large accumulations of I^{131} in the

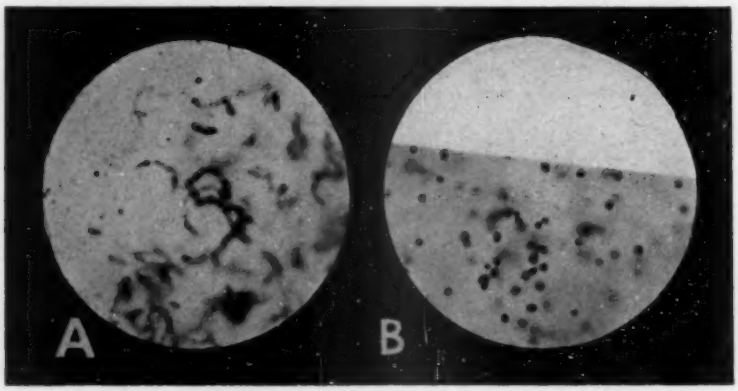

FIG. 3. *A*, *Mycobacterium tuberculosis* after a ninety-six hour exposure to 300 microcuries of I^{131}. Ziehl-Nielsen stain. ×1250. *B*, radioautograph of *A* on Eastman NTB 25 micron uncoated plate. ×1250. The radioautographs demonstrated that the isotope was present in the organisms in sufficient quantity to affect the plate. At the magnification used the depth of focus was decreased to the extent that all of the affected silver granules could not be focused in the same plane, therefore these radioautographs are not as satisfactory as those done on colonies at lower magnifications.

region of the bladder immediately (thirty to sixty minutes) after the injection and most of the I^{131} in the thyroid area at the twenty-four hour period and thereafter. This is the expected or predicted distribution of the I^{131}.

In animals 5–12 inclusive the radioactive iodine, which was taken up by the various fungi (pathogens and non-pathogens) and tubercle bacilli prior to injection, did not follow the same distribution as uncombined inorganic I^{131}. Instead of going to the thyroid as in the controls, the iodine apparently remained within the micro-organisms, which were picked up by the reticulo-endothelial system, until these were destroyed.

Alternaria containing I^{131} was injected intravenously into animal 5 and, as shown in Table 1, did not go directly to the thyroid. The animal was sacrificed in fourteen days and Geiger counts on the viscera showed radioactivity in the thyroid only. Cultures from liver, spleen and lung failed to show evidence of the injected organism. Apparently, when the *Alternaria* was destroyed by the macrophages in the liver and spleen, the iodine was released and then went to the thyroid gland.

The ability of fungi to absorb and to retain the radioiodine varies with the genera; therefore, it was not always possible to give the same quantity of radioactivity in a tolerable quantity of suspension of the organism. The quantitative uptake and retention of radioactive isotopes by micro-organisms has been the subject of a previous publication and this study is being continued. For the purposes of this paper, the quantitative value of the dosage is not significant since our purpose was to study: (1) the initial localization of the radioactivity, (2) its subsequent distribution and (3) its final disposition in the animal body.

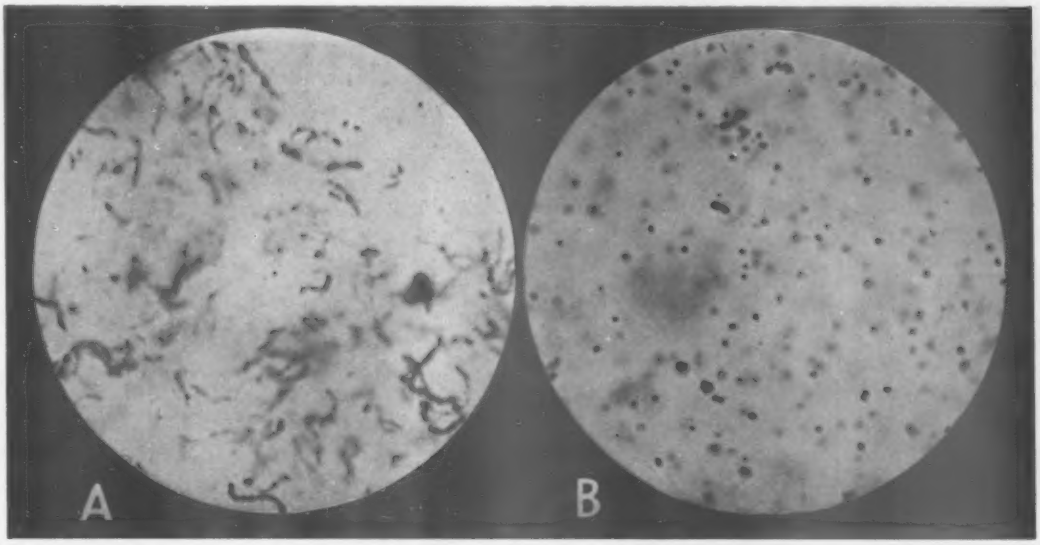

Fig. 4. *A* and *B*, same as Figure 3 except ×1500.

For example, animal 6 and 7 are the same dog employed twice in two different experiments to contrast the rates of exchange of radioiodine in the case of *Fusarium* and of *Alternaria*. As No. 6, this animal was injected with *Fusarium* containing I^{131}. Nine months later this same animal was injected with *Alternaria* prepared in the same manner. As will be seen from Table 1, the *Alternaria* retained the radioactive tracer in the liver and spleen for a much longer period of time than did the *Fusarium*, although both caused its retention in these organs much longer (days)

than the normal retention period for simple inorganic radioiodine, as shown in the control animals.

In animal 8 the *Alternaria*-radioiodine study was repeated in a different animal and the results in animal 7 were confirmed.

The technique of injecting significant quantities of suspensions of the micro-organisms constituted a problem in itself, particularly when a high specific radioactivity within the organism made standard procedures of colloid preparation impractical or difficult. In general, it was demonstrated that 5 milliliters of a suspension of micro-organisms having just a faintly opalescent appearance and containing about 5 milligrams of organisms per milliliter was the maximum which could be administered safely.

Animal 9 was the only one killed unintentionally. In this case a suspension of *Fusarium* mycelium, which had been cleared as completely as possible of spores, was injected. It was not found possible to reduce the particle size of this suspension to a desirable level and visible small clusters were present. This animal went into shock and died immediately. Multiple emboli were found in the lungs at autopsy. It was demonstrated that the clusters of mycelia had served as nuclei for the emboli.

In animal 10 *Oospora* containing I^{131} was injected and the resulting iodine uptake was demonstrated to be altered in a manner similar to that in the case of *Alternaria*.

In animal 11 *Blastomyces dermatitidis* containing I^{131} was injected intravenously. Geiger counter examination revealed altered I^{131} distribution, the activity being found in the chest, liver and splenic areas. This animal died at the end of twenty-one days of systemic blastomycosis as proved by cultures of lung, liver, spleen and nasal secretion and by microscopic sections. Splenic aspirations on this animal during life were positive for *Blastomyces* on culture and were radioactive for a period of eight days. After fourteen days there was no detectable radioactivity in any area. Cultures for organisms other than *Blastomyces* were negative throughout. At no time during this experiment was a significant concentration of radioiodine built up in the thyroid.

A partial study was also conducted with *Actinomyces asteroides*, *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Candida albicans* and *Sporotrichum schenckii*. Only one experiment could be conducted with these organisms and, hence, the results are not considered conclusive. There was no indication that the behavior of the radioiodine present in these organisms gave any result different from that described with the *Blastomyces*.

In contrast to the non-pathogens, the *Blastomyces* was not destroyed by the reticulo-endothelial system, but continued to multiply and eventually killed the host. It is demonstrated by this experiment that the pathogen alters the iodine distribution in a manner different from the non-pathogen in that no significant concentration of radioiodine is released to be collected in the thyroid.

In animal 12 *Mycobacterium tuberculosis* (human) containing I^{131} was administered intravenously. Radioiodine appeared quickly in the thyroid but in weak concentration, representing about 10 per cent of the dose administered. This probably represents some actual destruction of the organism or an attack upon its waxy capsule, since the preparation had been washed clean of radioactivity before administration. After the third day there was a decrease in the activity of the thyroid to a negligible level but a continued, significant radioactivity was demonstrable in the liver area. This animal was sacrificed and found to have a miliary tuberculosis involving the lungs, liver, spleen and tracheobronchial lymph nodes. The organism was recovered on postmortem culture of all of the above organs. The significance of this experiment lies in the fact that it was demonstrated that the radioactive tracer was retained in the area most affected by the tuberculosis infection. These results may, in part, explain the fact demonstrated re-

peatedly in this laboratory, that tuberculous lesions simulate in some respects the iodine metabolism of aberrant thyroid tissue in the human. In any case, it demonstrates a practical technique for tracing the path of these organisms.

Many check experiments were performed in order to be sure that the results presented were not due to some factor other than those to which they are ascribed. For example, animal 13 was given *Fusarium* intravenously one week prior to injection of I^{131}. A standard tracer dose of radioiodine was administered at the end of the week and was found to follow the standard pattern for a normal animal without any demonstrable abnormality. It is illustrated that neither the non-pathogenic *Fusarium* nor any minor lesions which it may have produced due to mechanical obstruction or other possible side effect influenced the course of the radioactive tracer. Since it might not be expected that active *Fusarium* would still be present to any significant extent in the animal body at the end of one week, this experiment was repeated with a suspension of *Fusarium* administered fifteen minutes before the administration of 100 microcuries of radioactive iodine. Geiger counter studies were started at the end of an additional ten minutes and continued throughout the next thirty minutes. Serial studies were conducted in the usual manner thereafter.

In Table 1 only one entry is made representing the first day; this is the average count of the first day. By the second day there was only the normal distribution of radioactivity in the liver and spleen which gave 550 and 560 counts per minute respectively compared to 1,450 for the thyroid. On the third day the thyroid count was 1,800 counts per minute, while the spleen gave 150 and the liver 130. The soft tissue showed a normal rate of decrease throughout. There was no excess of activity over the site of injection and counts over both shoulders were identical. It was demonstrated that the injection of *Fusarium* had absolutely no effect upon the distribution of the radioactive iodine injected into the same vein fifteen minutes later.

CONCLUSIONS

1. The distribution of pathogenic and non-pathogenic organisms administered intravenously can be followed by first making the organism radioactive.

2. Relative rates of destruction of non-pathogens are demonstrated by the decrease in radioactivity of the reticuloendothelial system and increase in radioactivity of the thyroid when I^{131} is used as the tracer.

3. The relative indestructibility of the pathogens as compared to the non-pathogens is illustrated by the retention of the radioactive tracer in the lesions of blastomycosis and tuberculosis.

4. Various techniques, including radioautographs, for the study of these effects are presented.

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DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

PORTABLE PROJECTOR FOR ROENTGENOGRAMS*

By RAYMOND A. DILLON, M.D., *and* WILLIAM P. MURPHY, JR., M.D.
BOSTON, MASSACHUSETTS

THE authors have long felt that some type of apparatus to project full sized, original roentgenograms on to a large screen would be of utmost value wherever roentgenograms are to be demonstrated. For some time one of us has attempted to show roentgenograms to large groups at hospital staff meetings, roentgenologic conferences, professional societies and to classes of medical students. Conventional methods have left much to be desired. All but the grossest detail on the film is lost to those beyond the first few rows.

The use of the view box, with all of its recent improvements, is obviously unsatisfactory both to the audience and to the speaker. Often the field under discussion cannot be seen satisfactorily even with a pair of binoculars. Reproducing films on a lantern slide not only entails much delay and expense, but the result is often disappointing. This is partially due to the photographer not knowing what range of tones to reproduce, and to the physical impossibility of reproducing on a single-coated emulsion the full scale of tones present on a properly exposed double-coated roentgen film.

After much thought over a period of years, and experimentation with numerous methods of projection, the present apparatus was constructed. Numerous light sources were tried and many condenser equipment and preliminary condensers. A 45 degree mirror in the large section directs a horizontal beam up through the field lenses and film. The light is converged on to the overhead projection lens and is reflected to the screen by a surface-coated mirror. The height of the overhead projecting system is such that a person walking in front of the apparatus will not interfere with the image on the screen.

Fig. 1. The roentgenogram to be demonstrated is placed on the field condenser. The small section on the right contains the light source, cooling

* Shown in an exhibit at the Forty-ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept 14–17, 1948.

systems were investigated. A major obstacle has always been the unavailability of commercially made components. After the present optical system was decided upon, most of the lenses had to be individually designed and ground. Plastic lenses have proved unsatisfactory.

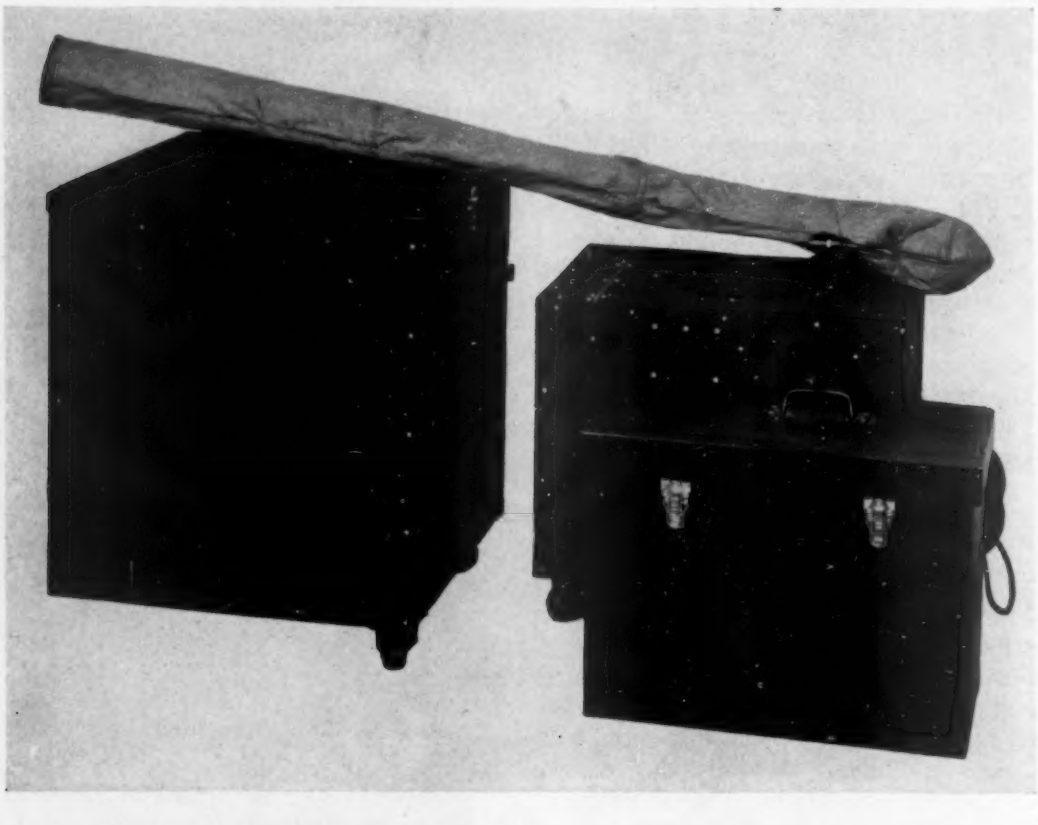

FIG. 2. In spite of the weight and size, the equipment is relatively easy to transport because it readily separates into four main components. When taken apart, metal doors are arranged to fit over the openings and protect the various lenses. Rubber wheels allow the individual sections to be rolled along the floor, or the whole apparatus assembled can be pushed from room to room. Disappearing handles allow the sections to be easily carried.

Because of the large size of a 14 by 17 inch film, as compared with a 35 mm. or standard lantern slide, this type of projector must, of necessity, have large physical dimensions. Some of the lenses weigh seventy pounds each. To save weight, many of the mounts, and other metal parts, are cast aluminum.

In spite of the weight and size, the equipment is relatively easy to transport because it readily separates into four main components. When taken apart, metal doors are arranged to fit over the openings and protect the various lenses. Rubber wheels allow the individual sections to be rolled along the floor, or the whole apparatus assembled can be pushed from room to room. Disappearing handles allow the sections to be easily carried.

The smaller section contains the light source, cooling equipment and preliminary condensers. These are mounted in a vertical position. The larger section contains the field condenser system which is mounted horizontally. It is protected by a piece of plate glass directly above, on which the film to be projected is placed. In this section

is a mirror placed at 45 degrees to the optical axis which serves to redirect the horizontal beam up through the field lenses. The light beam, having passed through the field condenser and the film, now converges to pass through the projection lens mounted in the overarm. It is reflected toward the screen by a second surface-coated mirror.

The instrument may be placed in any upright position relative to the screen. The overhead reflecting mirror can be tilted up or down, as well as turned through 360 degrees. A sharp focus is obtained by racking the projecting lens up and down. The projecting lens is a specially designed achromat of large numerical aperture. Due to the large size of the image to be projected, great difficulty was encountered in designing lenses to provide a sharp focus throughout the field, but this was finally accomplished.

Since the apparatus was meant to be used in many different institutions, the entire source and cooling equipment were constructed so that they could be supplied from the average electrical outlet and not require special wiring or special kinds, or amounts, of electricity.

In use, the film to be demonstrated is simply placed on the field condenser aperture and the electricity switched on. At a distance of 30 feet, the image fills a 6 by 8 foot screen. Separate case roentgenograms are easily shown and the entire teaching collection of a department is made immediately available for routine demonstrations. No detail is lost in projection for the original film is used as the image. Multiple films, such as sinus views or spot films, may be shown simultaneously. For example, four 5 inch diameter views may be projected at once. The lecturer may point out detail on the film and a clear image of the pointer used will be transmitted to the screen. Marks made on the film will be clearly shown. Cleared film or white paper may be used for diagram and any drawings or writing, such as one would make on a blackboard, will be seen greatly magnified. Photographs may be enlarged on roentgen-ray film and likewise projected.

The greatest problem in projection of roentgenograms has always been the tremendous amount of heat produced by the light source and transmitted to the film. Using any one of the innumerable possible projection methods, it is an easy matter to obtain almost any amount of light on the screen simply by increasing the amount of light at the source, but the film is likely to catch on fire. The great difficulty is that there is no efficient method of changing electrical energy into visible light. The best commercial projection bulb is less than 20 per cent efficient. This means that about 80 per cent of the electrical energy is turned into heat and transmitted with the light. This projector uses a 1,500 watt bulb and thus there is produced about the same amount of heat as two hot plates on an electric stove. This great amount of heat is effectively separated from the visible light by differential reflection and absorption so that a film may be left on the machine indefinitely without damage of any kind.

During the past year, the apparatus has been used with many different groups, large and small, and in a variety of rooms and auditoriums; both day and night and with an assortment of screens. Brilliance and detail have been most satisfactory.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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EDITORIALS

INTUSSUSCEPTION

THE function of the radiologist in the care of infants suspected of having intussusception may be considered in both its diagnostic and therapeutic aspects.

It has been stated that clinical diagnosis of intussusception in infants is usually simple with the recognition of colicky abdominal pain, palpation of an abdominal mass, and the observation of blood in the stools. Ladd and Gross,[1] in their authoritative text, report that the roentgen examination was resorted to in only 25 of 484 cases, or in about 5 per cent of the cases of intussusception observed at the Boston Children's Hospital. There is general agreement that the most important factor in a successful outcome of these cases is early diagnosis and treatment. It is evident that the earlier the diagnosis is to be made, the less characteristic the symptoms will be. Colicky abdominal pain is not always easy to recognize in infants and may be seen in a variety of conditions. Likewise, abdominal masses are difficult to palpate in a distressed infant and different observers may report differing impressions. Bleeding would seem to be a rather late manifestation when the intussusception has been present for some time and considerable vascular congestion has already developed. Signs of bowel obstruction are an even later manifestation and when this has occurred the bowel is often gangrenous and the intussusception irreducible. Mistakes in diagnosis are made and the procedure of exploratory laparotomy before other methods of investigation have been exhausted is to be deplored and is fortunately falling into disuse in recent years. The roentgen examination of the colon by barium enema provides a rapid, simple, accurate and reliable means of diagnosis in ileocolic intussusception, which is by far the most common type of intussusception in infants. If an early and accurate diagnosis is to be made it would seem that this procedure should be much more frequently employed.

The treatment of intussusception in this country has been almost entirely surgical. Ladd and Gross mention non-operative methods only to condemn them as dangerous and unwarranted. However, observers have reported the spontaneous reduction of intussusception and reduction has apparently occurred under ether anesthesia. Reduction has also been noted not infrequently following a diagnostic barium enema. It is reasonable to suppose that if an intussusception is recognized early a reduction could easily be accomplished by a gentle retrograde pressure such as may be exerted by a barium enema. The use of enemas of various types in the treatment of intussusception has a long history antedating the use of surgery. The barium enema administered under roentgenoscopic control and controlled hydrostatic pressure is, of course, a great improvement over other forms of treatment by enema. This method has been widely employed abroad with apparent success. The monograph of Hans Hellmer[2] on "Intussusception in Children; Diagnosis and Therapy with Barium Enema" records the experience at the University Clinics in Lund, Sweden, with 162 cases of intussusception observed in a period of fourteen years. Reduction was accomplished by barium enema in 80 per cent of

[1] Ladd, W. E., and Gross, R. E. Abdominal Surgery of Infancy and Childhood. W. B. Saunders Company, Philadelphia, 1947.

[2] Hellmer, Hans. Intussusception in Children; Diagnosis and Therapy with Barium Enema. *Acta radiol.*, suppl. 65, 1948.

the cases. There were no deaths in these cases. Among the 30 cases where operation was necessary there were 9 deaths. Lindberg and Morales[3] have more recently reported the successful treatment by barium enema of acute early intussusception in 18 consecutive cases in infancy. They emphasize the importance of early diagnosis for the success of this form of treatment. All of their patients had symptoms of less than twelve hours' duration and in 14 the symptoms had been present for less than six hours. The recent report by Ravitch and McCune[4] from the surgical department of the Johns Hopkins Hospital will undoubtedly stimulate the non-operative treatment of intussusception in this country. As surgeons they favor treatment by barium enema and record data showing that the mortality and morbidity in intussuscpetion have been much reduced since the treatment has been primarily by barium enema. They report 33 cases treated primarily by barium enema with no deaths and in 24 of these, or 73 per cent, reduction was accomplished by the barium enema alone. They provide convincing answers to the objections commonly raised to this method of treatment. The time required for the barium enema is not prohibitive and should not cause a serious delay if operation proves to be necessary. The accuracy of diagnosis of complete reduction by barium enema is high but the possibility of the rare ileo-ileal intussusception must be kept in mind. Recurrence of the intussusception is apparently higher following reduction by barium enema (16.5 per cent according to Hellmer) than following surgery (2 per cent according to Ladd and Gross). As for the lesions which may be responsible for the intussusception (Meckel's diverticulum, intestinal polyp or other tumor, and duplication), these are rare (5 per cent in the series of Ladd and Gross) and are better dealt with at a later operation than at the time the intussusception is reduced. As for possible rupture of the bowel, Ravitch and McCune state that it may occur during the course of reduction whether by hydrostatic pressure or manual manipulation but is much less likely to occur during a barium enema "since less force is employed and that force is diffusely distributed."

If the intussusception has not been completely reduced by barium enema the surgeon's task will have been simplified as the manual reduction of an ileocecal intussusception is much simpler than the manual displacement of the small intestine from the distal colon requiring a wider exposure and a more time-consuming manipulation.

The treatment of intussusception offers a test and a challenge for the close cooperation and interdependence of the pediatrician, surgeon, and radiologist.

WILLIAM A. EVANS, JR., M.D.

[3] Lindberg, Gustaf, and Morales, Olallo. Treatment of acute intussusception by an enema of roentgenologic contrast medium. *Am. J. Dis. Child.*, March, 1949, *77*, 303–309.

[4] Ravitch, M. M., and McCune, R. M. Reduction of intussusception by barium enema; clinical and experimental study. *Ann. Surg.*, 1948, *128*, 904–917.

THOMAS S. STEWART
1876–1949

DR. THOMAS S. STEWART, a member of the American Roentgen Ray Society since 1903 and one of the pioneers in roentgenology in Philadelphia, died on February 19, 1949, at the age of seventy-three. The following notice was written by Dr. George E. Pfahler for publication in the program of the Philadelphia Roentgen Ray Society:

IN MEMORIAM DR. THOMAS S. STEWART

"We have lost another distinguished pioneer in roentgenology. Dr. Thomas S. Stewart was one of six roentgenologists who met in Dr. Charles Lester Leonard's office and founded the Philadelphia Roentgen Ray Society in 1905. Dr. William S. Newcomet and I are the only two of these pioneers remaining.

" 'Tom Stewart' as we called him was born August 2, 1876, and died February 19, 1949, at the age of seventy-three. His death is attributed to a series of heart attacks, the first of which occurred New Year's Eve, 1948.

"He retired from radiology in 1928. He did, however, retain his membership in both the Philadelphia and American Roentgen Ray Societies until the time of his death. He was an active member of the Academy of Natural Sciences and was Curator of the Microscopic Section. He was also a Fellow of the Royal Microscopical Society of London, and a life member of the Historical Society of Pennsylvania, and a member of the Philadelphia County Medical Society, the Medical Club of Philadelphia, and of the American Medical Association.

"He had his preliminary training and experience in association with Dr. Leonard at the University of Pennsylvania Hospital. During the celebration of the 50th Anniversary of the discovery of the Roentgen Rays, he and I helped to collect some of the x-ray tubes and induction coils that were used in Philadelphia as early as 1896. In 1905, and for a number of years thereafter, the Philadelphia Roentgen Ray Society met serially at the offices of the six members, at which time we demonstrated to each other any new apparatus, new technique or new observations. It was really a close fellowship. Tom was loved by all of us and was well informed."

GEORGE E. PFAHLER, M.D.

PERCY JOSEPH DELANO
1899–1949

PERCY JOSEPH DELANO died suddenly on January 13, 1949. Death was due to severe burns accidentally sustained in his home.

Dr. Delano was born in Kewaunee, Illinois, September 21, 1899. He spent his boyhood in Kewaunee and during the first World War served in the enlisted ranks of the Army of the United States. He came to Chicago where he received his premedical education at Northwestern University and his M.D. degree from the University of Illinois in 1927.

Following graduation he interned at the

Cook County Hospital and later returned to that institution where he studied radiology under the late Dr. Maximilian J. Hubeny. He became Chief of the Department of Radiology at the West Suburban Hospital in Oak Park, Illinois.

Dr. Delano was very active professionally. He contributed numerous articles to the radiological literature. He was a diplomate of the American Board of Radiology; a member of the American Roentgen Ray Society, of the American College of Radiology, of the Radiological Society of North America and a Fellow of the Chicago Roentgen Society and of the American Medical Association. In addition to his professional activities he found time to write short stories which had been published in American and English magazines and to pursue his hobby, the violin and piano.

Dr. Delano will be remembered by his colleagues as a man who was extremely generous with his time and knowledge which he was always willing to share with the many who sought his advice.

Robert F. Stokes, M.D.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

AMERICAN RADIUM SOCIETY
Secretary, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: Ambassador Hotel, Atlantic City, N. J., June 5–7, 1949.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland Auditorium and Statler Hotel, Cleveland, Ohio, Dec. 4–9, 1949.

AMERICAN COLLEGE OF RADIOLOGY
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: Chalfonte-Haddon Hall, Atlantic City, N. J., June 5, 1949.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio, Annual Meeting: Atlantic City, N. J., June 8–10, 1949.

ALABAMA RADIOLOGICAL SOCIETY
Secretary, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

ARIZONA ASSOCIATION OF PATHOLOGISTS AND RADIOLOGISTS
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. Joseph Daversa, 603 Fourth Ave., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Hannan, Cleveland Clinic, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

COLORADO RADIOLOGICAL SOCIETY
Secretary, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

DALLAS-FORT WORTH ROENTGEN STUDY CLUB
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

EAST BAY ROENTGEN SOCIETY
Secretary, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

HOUSTON X-RAY CLUB
Secretary, Dr. Curtis H. Burge, 3020 San Jacinto St., Houston 4, Texas. Meets fourth Monday each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

IOWA X-RAY CLUB
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

KANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

LOUISVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
Secretary, Dr. C. E. Grayson, Medico-Dental Bldg., Sacramento 14, Calif. Meets at dinner last Monday, every second month, except June, July and August.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: May 20 and 21, 1949, Bedford Springs Hotel, Bedford, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Arthur Finkelstein, Graduate Hospital, 19th and Lombard St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
Secretary, Dr. A. A. J. Den, 1801 K St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Shirley-Savoy Hotel, Denver, Colo. August 18, 19, 20, 1949.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. C. J. Nolan, 737 University Club Bldg., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
Secretary, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. D. R. MacColl, 2007 Wilshire Blvd., Los Angeles 5, Calif.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. Harold L. Shinall, St. Joseph's Hospital, Bloomington, Ill.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon. 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, February 3 and 4, 1950.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

VIRGINIA RADIOLOGICAL SOCIETY
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-RAY STUDY CLUB OF SAN FRANCISCO
Secretary, Dr. W. F. Reynolds, University of California Hospital, San Francisco. Meets from January to July, 1949, at Lane Hall, Stanford University Hospital, and from July to December 1949, at San Francisco Hospital.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGIA Y FISIOTERAPIA
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. E. M. Crawford, 1535 Sherbrooke St., West, Montreal 26, Que. Meetings January and June.

SECTION OF RADIOLOGY, CANADIAN MEDICAL ASSOCIATION
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

SOCIÉTÉ CANADIENNE-FRANCAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East, Montreal, P. Q.

AUSTRALIAN AND NEW ZEALAND ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. Alan R. Colwell, 135 Macquarie St., Sydney, N.S.W.
Honorary Secretaries, State Branches:
New South Wales, Dr. E. W. Frecker, 135 Macquarie St., Sydney.
Victoria, Dr. T. J. Tyrer, 3 Lockerbie Court, East St. Kilda.
Queensland, Dr. J. Adam, 131 Wickham Terrace, Brisbane.
South Australia, Dr. B. C. Smeaton, 178 North Terrace, Adelaide.
Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

SOUTH AMERICA

SOCIEDAD ARGENTINA DE RADIOLOGIA
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY
Secretary, Dr. Arias Bellini.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

CESKOSLOVENSKÁ SPOLEČNOST PRO RÖNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

WARSAW SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

MOSCOW ROENTGEN RAY SOCIETY
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
President, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano Torino, Italy. Meets biannually.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Annual Mid-Summer Meeting of the Rocky Mountain Radiological Society will be held in Denver, Colorado, at the Shirley-Savoy Hotel on August 18, 19 and 20, 1949. As will be noted on the program, there is to be a symposium and conference on medical economics, particularly as they pertain to radiology. Also, there will be a symposium on the lesser circulation and on chest diseases, as well as a symposium on radioactive isotopes. Further information concerning the meeting may be obtained from the Secretary, Dr. Maurice D. Frazer, Lincoln, Nebraska. The following program has been arranged:

Thursday Morning, August 18, 1949

9:30–11:00 Registration.

11:00–12:00 "Symposium on Ethics of Economics in Radiological Practice," James P. Kerby, M.D., Salt Lake City, presiding.

12:30 Round Table Luncheon

"Discussion of Ethics and Economics," James P. Kerby, M.D., Salt Lake City, presiding.

Thursday Afternoon, August 18, 1949

2:00 Howard B. Hunt, M.D., Omaha, presiding.

President, Rocky Mountain Radiological Society.

Address of Welcome, President Colorado State Medical Society.

2:10 Paul R. Weeks, M.D., Denver, presiding.

"Pathology of Congenital Heart Disease," Harold D. Palmer, M.D., Denver.

2:45 "Angiocardiography," J. E. Miller, M.D., Dallas.

3:30 "Hypertension of the Pulmonary Circulation," C. Allen Good, M.D., Rochester Minnesota.

4:00 "The Auxiliary Heart," W. Walter Wasson, M.D., Denver.

4:45 "Discussion"—John B. Grow, M.D., Denver. Carl J. Josephson, M.D., Denver. Wm. B. Condon, M.D., Denver.

5:00 Executive Session.

Thursday Evening, August 18, 1949

8:00 Joint Meeting with the Medical Society of the City and County of Denver.

Frederick H. Good, M.D., Denver, President of the Medical Society of the City and County of Denver.

Guest Speakers

Paul C. Swenson, M.D., Philadelphia, "Problems in the Roentgen Examination of the Gastrointestinal Tract."

Charles L. Martin, M.D., Dallas, "The Treatment of Intra-Oral Cancer."

Friday Morning, August 19, 1949

9:00 Thomas B. Bond, M.D., Ft. Worth, presiding.

Vice President, Rocky Mountain Radiological Society.

"Double Contrast Study of the Colon," Robert D. Moreton, M.D., Temple, Texas.

9:20 "Lesions of the Small Intestine," C. Allen Good, M.D., Rochester, Minnesota.

9:50 "Bronchography in Carcinoma of the Lungs," John W. Walker, M.D., Kansas City.

10:10 "Discussion"—Ira H. Lockwood, M.D., Kansas City. John T. McGreer, M.D., Lincoln.

10:25 "Diagnostic X-ray Procedures at the Time of Labor," Paul C. Swenson, M.D., Philadelphia.

11:00 "Uterosalpingography in the Diagnosis and Treatment of Sterility," Charles L. Martin, M.D., Dallas.

11:45 "Discussion"—Kenneth D. A. Allen, M.D., Denver. Charles G. Freed, M.D. E. Stewart Taylor, M.D.

12:30 Round Table Luncheon

"Discussion of Diagnostic Problems," Wm. W. McCaw, M.D., Greely, Colorado, presiding.

Friday Afternoon, August 19, 1949

2:00 Kenneth D. A. Allen, M.D., presiding. President-Elect, Rocky Mountain Radiological Society.

"Characteristics, Instrumentation and Safe Handling of Radioisotopes in Medical Practice, Paul G. Aebersold, Ph.D., Oak Ridge, Tennessee.

2:45 "Application of Radiophosphorus in Radiological Practice," Capres S. Hatchett, Amarillo, Texas.

3:15 "Studies on the Genesis and Function of Neoplasms of the Thyroid with Modern Tools," R. W. Rawson, M.D., New York.

4:00 "The Treatment of Hyperthyroidism

by Radioiodine," Earl R. Miller, M.D., San Francisco.

4:45 "Discussion"—Thad P. Sears, M.D., Fort Logan, Colorado. Charles F. Ingersoll, M.D., Fort Logan, Colorado.

5:00 Executive Session.

Friday Evening, August 19, 1949

7:00 Social Hour.

7:30 Informal Banquet, Howard B. Hunt, M.D., presiding.

8:45 Address: "Illustrated Travelogue Through Scandinavia and Great Britain," Hamilton Berg, M.D., Bismarck, North Dakota.

Saturday Morning, August 20, 1949

9:00 Installation of Officers, Howard B. Hunt, M.D., presiding.

9:10 M. Lowry Allen, M.D., Salt Lake City, presiding, Vice President, Rocky Mountain Radiological Society.

"Epidermoid Carcinoma of the Bulbar Conjunctiva," Edward J. Meister, M.D., Denver.

9:30 "Radiotherapy in Brain Tumors," Galen M. Tice, Kansas City.

10:00 "Cerebral Angiography," Earl R. Miller, San Francisco.

10:30 "Discussion"—Ophthalmologist and Neurosurgeon.

10:45 "High Voltage Radiography," E. Dale Trout, Ph.D., Milwaukee.

11:00 "Short Distance Radiography," James W. Lewis, M.D., Colorado Springs.

11:15 "Relation of the Atomic Energy Program to Medical Practice and Research," Paul G. Aebersold, Ph.D., Oak Ridge, Tennessee.

11:35 "Some Newer Aspects of Cancer Research," R. W. Rawson, M.D.

11:55 "Discussion"

12:30 Round Table Discussion of Therapy Problems, A. M. Popma, Boise, Idaho, presiding.

Saturday Afternoon, August 20, 1949

4:00 Annual Picnic—Pine Gables Ranch.

THIRD INTER-AMERICAN CONGRESS OF RADIOLOGY

The Third Inter-American Congress of Radiology (Tercer Congreso Inter-americano de Radiologia) will take place in Santiago, Chile, November 11 to 17, 1949, inclusive. The meetings will take place in the University of Santiago and in Viña del Mar, a summer resort near the capital.

There will be a scientific program and exhibit of radiographic documents, technical-commercial exhibits.

The official topics of the Congress will be the following:

A. "Radiological Exploration of the Cardiovascular System with Opaque Material." This official relation should refer essentially to the radiological exploration of the heart and great blood vessels. Inclusion in the official presentation of the exploration of the peripheral vascular system will be optional.

B. "Diagnosis and Simple Radiological Exploration of the Skull." With the object of facilitating its consideration, this subject has been divided into three official presentations:

(1) a. Skull in general.
b. Sella turcica.
(2) c. Orbits.
d. Paranasal cavities.
(3) e. Temporal bone.

These official presentations should constitute a short exposition, read without introducing cases, being a résumé of the experience in that country.

Official Essayists and Collaborators may bring all the material they wish, preferably full-size originals, for exhibition in the Scientific Exhibits. In view of the nature of this subject, the Executive Committee requests that collaborations be fundamentally objective, and insists on the exhibit, making the verbal part as brief as possible.

C. "Radiation Treatment of Cancer of the Tongue."

D. "Radiation Treatment of Cancer of the Cervix."

Official presentations on these two subjects should comprise essentially the following parts:

1. Radiotherapy technique.
2. Immediate and subsequent reactions, and,
3. Case reports illustrating the clinical degree and the histological type of cancer.

For the above topics there will be assigned one major relator and one discussant, but there will be opportunity for a number of so-called "free papers" or topics of the authors' choice. We need volunteers

for the major papers and for the free papers. Scientific exhibits are also desirable.

The undersigned has full particulars as to the details of the exhibits and how they should be prepared. Those who propose exhibits will please communicate with the undersigned.

For demonstration of the radiographic material there has been arranged a permanent exhibition in the same location as the meeting to be held in Santiago.

In arranging the program, free time has been set apart for various functions of social and touristic order for the pleasure of the visitors.

About two hundred and fifty radiologists were enrolled in the Second Inter-American Congress of Radiology which took place in Havana, Cuba, in November, 1946, and it is hoped that an equally good attendance may be counted upon for the Santiago meeting.

While the trip may seem long, those who are pressed for time may make the trip by air; those with more time will find it enjoyable to travel by boat, part or all of the way. A round trip of South America makes a delightful journey; for instance, going down via the Atlantic coast, visiting Havana, San Juan, and the principal ports in Brazil, Uruguay and the Argentine, then across the Andes by train or by plane to Santiago, Chile. After the meeting one may return via the Pacific coast by steamer through the Panama Canal or by plane. If the traveler has time, most pleasant visits may be made in Guatemala, Yucatan and perhaps in the capital city of Mexico. Various modifications of these trips are available, so that the absence may be as long as a couple of months or as short as twenty-one days. Southern Chile is noted for its tourist attractions.

Travel arrangements may be made individually or by your nearest travel agent. The McGuire Travel Agency, 333 North Michigan Avenue, Chicago 1, Illinois, has been serving our committee very acceptably. The travel agency should make all room reservations, but no matter how one travels, it is requested that the undersigned, as regional secretary, be informed.

Adherents to the Congress should send in a check for twenty dollars which will entitle him to the Proceedings of the Congress whether or not he attends the meeting. One may be a member without attending.

Of course, passports will have to be arranged and the necessary visas obtained. The travel agency will be of much assistance in this regard. Inquiries may also be addressed to us.

James T. Case, M.D.
Regional Secretary for the
United States
55 East Washington Street
Chicago 2, Illinois

CANCER TEACHING DAYS

A Cancer Teaching Day was presented on May 25, 1949, at Albany, New York, under the auspices of the Medical Society of the County of Albany, Albany Medical College, Medical Society of the State of New York, Third District Branch of the Medical Society of the State of New York, and the New York State Department of Health, Bureau of Cancer Control. The following papers were given at the afternoon and evening sessions:

The Biological Differentiation of Malignant Tissue. Harry S. N. Greene, M.D., New Haven, Conn.

Cancer: The Problem of Early Diagnosis. 16 mm. color, sound movie.

Cancer in Childhood. Harold W. Dargeon, M.D., New York, N. Y.

The Diagnosis and Treatment of Sarcomas of the Soft Parts. George T. Pack, M.D., New York, N. Y.

A Cancer Teaching Day was also presented on May 25, 1949, at Binghamton, New York, under the auspices of the Medical Society of the County of Broome, Medical Society of the State of New York, Sixth District Branch of the Medical Society of the State of New York, Binghamton City Department of Health, New York State Department of Health, Bureau of Cancer Control. The following papers were given at the afternoon and evening sessions.

Cancer: The Problem of Early Diagnosis. 16 mm. color, sound movie.

The Significance of Enlarged Lymph Nodes. Henry D. Diamond, M.D., New York, N. Y.

Clinical and Roentgenographic Diagnosis of Oral Tumors. Harold A. Solomon, D.D.S., Buffalo, N. Y.

Gastric Cancer—Newer Diagnostic Methods. William A. Cooper, M.D., New York, N. Y.

The Significance and Management of Abnormal Vaginal Bleeding. Clyde L. Randall, M.D., Buffalo, N. Y.

SYMPOSIUM ON MODERN PHYSICS

A symposium consisting of thirty-two lectures on Modern Physics will be given at Oak Ridge, Tennessee, from August 22 to September 2, 1949, under the sponsorship of the Oak Ridge National Laboratory and the Oak Ridge Institute of Nuclear Studies.

The lecture staff will be drawn from among the well-known physicists who are expected to spend the summer at the Oak Ridge National Laboratory. Among these are: Professor S. M. Dancoff, University of Illinois; Professor J. G. Daunt, Ohio State University; Professor Eugene Feenberg, Washington University; Professor Hubert M. James, University of Illinois; Dr. Alvin M. Weinberg, Oak Ridge National Laboratory. Professor N. Kurti, of Oxford University, also will be a lecturer.

The lectures will include such topics as the current status of meson theory, the new quantum electrodynamics, recent progress in low temperature physics, declassified nuclear reactor theory, and classical nuclear physics. The lectures will be in the nature of a progress report to physicists in general rather than research reports to individuals within highly specialized fields.

In addition to the physics staffs in Oak Ridge, the lectures will be open without charge to physics department staff members and graduate students in physics in the South and elsewhere and to individuals in related fields. The series is being offered primarily for physicists from Southern universities but it is open to others insofar as facilities permit.

Additional information may be obtained from the University Relations Division of the Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tennessee.

COURSE ON ONCOLOGY

A Course on Oncology—New Aspects will be given at the University of California Medical School, the Medical Center, San Francisco, California, September 12, 13 and 14, 1949, the Officers of Instruction being from the University of California Medical School. The course is open only to graduates of medical schools approved by the Council on Medical Education and Hospitals of the American Medical Association. The fee for the course is $40.00, payable at the time of enrollment, either by check or money order made payable to *The Regents of the University of California*. Information concerning the course may be obtained by writing to Stacy R. Mettier, M.D., Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22, California.

RESEARCH FELLOWSHIPS—THE AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians announces that a limited number of Fellowships in Medicine will be available from July 1, 1950–June 30, 1951. These Fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in Internal Medicine. Assurance must be provided that the applicant will be acceptable in the laboratory or clinic of his choice and that he will be provided with the facilities necessary for the proper pursuit of his work. The stipend will be from $2,200 to $3,200. Application forms will be supplied on request to The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., and must be submitted in duplicate not later than October 1, 1949. Announcement of awards will be made November, 1949.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

THE TREATMENT OF MALIGNANT DISEASE BY RADIUM AND X-RAYS: BEING A PRACTICE OF RADIOTHERAPY. By Ralston Paterson, M.C., M.D., F.R.C.S.E., D.M.R.E., F.F.R., Christie Hospital and Holt Radium Institute, Manchester, England. Cloth. Pp. 622, with numerous drawings, photographs, tables and roentgenograms. Baltimore: Williams and Wilkins Company, 1948.

Among the numerous recent publications on various phases of radiation therapy and radiation effects, radiologists and particularly radiotherapists will welcome this work by Dr. Paterson. Its more than six hundred pages contain a complete description of the basic principles underlying radiotherapy (both roentgen rays and radium), as well as a large section on specific applications to carcinoma and other malignant diseases involving various regions of the body. The plan of the book is not complicated. The discussion is given in straightforward, clear language, illustrated by numerous drawings, photographs and roentgenograms. It is really radiotherapeutic practice, setting forth the principles and practices of the Radium Institute in Manchester, England, which is now part of the Christie Cancer Hospital and the Holt Radium Institute. The detail of the text is sufficiently comprehensive without achieving encyclopedic proportions.

The author does not mean to imply that the methods and ideas which he presents are essentially the most desirable or the only methods. He realizes that there are many alternative, equally well-founded approaches to the various problems. Rather than a complete textbook or a summation of the present status of radiotherapy, the author prefers that his work be regarded as a statement of radiotherapeutic practice specialty, which has resulted from a reasonable combination of the various procedures which have been well tested. Many of the major issues are still in the balance such as the nature of the lethal effect of irradiation on normal and malignant cells; the factors determining radiosensitivity; the real influence of time and intensity factors, and the biological significance of wavelength.

The first three chapters of the book set forth the particular principles on which the Manchester methods are founded. No doubt there will be changes as the result of further research and experience. The author properly states that it is impossible today to make any justifiable distinction between roentgen therapy and radium therapy. The principles of the two modalities are identical, differing only in certain factors dependent upon the origin of the two forms of radiation.

The author has taken for granted that the reader will have a knowledge of the physics of radiation, and starts with gamma rays after they have left the needle or tube and the roentgen rays as a beam of radiation on the patient's side of the filter. The author calls attention to the fact that in this book he has not been so directly concerned with the curability or otherwise of cancer but rather with an evaluation of radiotherapy as a method of treatment.

In the opinion of the reviewer this work is remarkably well done. It seems that every radiotherapist would need a copy of the book.

JAMES T. CASE, M.D.

RADON: ITS TECHNIQUE AND USE. By W. A. Jennings, B.Sc., A. Inst. P., Physicist to the Royal Northern Hospital and Prince of Wales's General Hospital, Joint Radiotherapy Centre, and S. Russ, C.B.E., D.Sc., F.Inst.P., Formerly Physicist to the Middlesex Hospital, London. Cloth. Price, 18s. Pp. 222, with 12 pages of half-tones and 49 figures. London: John Murray, 1948.

As stated in the preface, this book has been written as a book of reference on the subject of radon. It consists of three parts.

Part I considers the disintegration series from radium to lead, the general properties of radon and a broad description of its use in medicine, biology and industry.

Part II is an exhaustive treatment of the extraction and purification process, followed by an excellent discussion on the problems encountered in a Radon Center designed primarily to supply the needs of an exacting clinic.

Part III covers tumor dosimetry in a concise

but adequate manner; medical considerations are very briefly dealt with in a chapter by Mr. T. A. Green.

The shortcomings of this book are few; its merits are many. Among the first are lack of better reference to other types of radon plants described in the literature, omission of discussion on the subject of radiation protection, and omission of bibliography to the chapter on medical considerations. Its merits are reflected in the clear exposition of the numerous problems encountered and the painstaking description of the techniques available for their solution.

Physicists and physicians concerned with the preparation and use of radon for clinical application will find this book very instructive and very valuable.

L. D. MARINELLI

STANDARDS FOR THE DIAGNOSIS AND TREATMENT OF CANCER. By The Cancer Committee of the Iowa State Medical Society. Second edition. Cardboard. Price, $1.00. Pp. 160. Athens Press, Iowa City, Iowa, 1948.

This publication in its first edition (1937) was among the first group of manuals to be published by various state medical societies. Because of the developments in the intervening eleven years, this revised edition has been issued. It is the aim of this compendium to make available, in a simple and concise form, for the use of physicians in general practice, what the authors believe to be the minimum standards of diagnosis and treatment of cancer. Because the clinical facts about the more common malignant growths are widely scattered throughout medical literature, this type of presentation in handbook style makes readily available the essential symptomatology, recognized methods of diagnosis and a survey of therapeutic procedures. After a brief dissertation on various general aspects of malignant diseases and on the importance of the family doctor in the cancer problem, the more common cancerous diseases are discussed in 32 sections varying from one to seven pages in length. The text of each section is concise and, in accord with the stated intention of the authors, the presentation is generally dogmatic in attitude. Within these limits, the discussion is adequate, informative and achieves the objective of the manual. An excellent feature is the clear separation of early signs and symptoms from late ones; this serves to emphasize again and again the importance of early diagnosis. It cannot be expected that the recommendations for treatment would meet with complete agreement by all the workers in the field. In general, they are sound although the implied suggestion that a simple mastectomy may be adequate surgery for an apparently early breast cancer would certainly not meet with general approval. Likewise most radiation therapists would not agree that irradiation of a cancer of the tonsil should be stopped as soon as the gross tumor has regressed. Another excellent feature is a bibliography (14 pages) of original articles and monographs which gives access to the voluminous literature on cancer.

ISADORE LAMPE, M.D.

THE THYROID AND ITS DISEASES. By J. H. Means, M.D., Jackson Professor of Clinical Medicine, Harvard University, and Chief of the Medical Services, Massachusetts General Hospital. Second edition. Cloth. Price, $12.00. Pp. 571, with 63 illustrations. Philadelphia: J. B. Lippincott Co., 1948.

This is the best available monograph dealing with diseases of the thyroid gland. It is comprehensive in its scope, and the material presented is based on the mature judgment of an author who has had a continuous and intense personal interest in this subject for many years. When the reviewer first went to Boston, in 1917, thirty-two years ago, James Howard Means, Jackson Professor of Medicine, Harvard University, the author of this volume, was actively engaged in a study of thyroid disorders at the Massachusetts General Hospital, and was sponsoring one of the first clinical laboratories for the determination of the basal metabolic rate, a procedure then in its infancy.

This volume, in 21 chapters and almost 600 pages, presents his views and opinions concerning all phases of the functions and maladies affecting the thyroid gland. In addition, chapters on "The Pathology and Tumors of the Thyroid" by R. W. Rawson and on "Surgery of the Thyroid" by Oliver Cope have been included.

The reviewer is not entirely in accord with all of the views expressed, but it is to be expected that in any field as extensive as thyroid diseases and one in which our knowledge is constantly advancing, there will be differences of opinion. For example, all observers are not in accord concerning the use of antithyroid drugs, one of the most important advances in this field in recent years. Dr. Means advocates a daily dose of propylthiouracil, the preparation of choice,

which varies from 75 to 300 milligrams, as a detoxifying medication. Furthermore, he appears to be uncertain as to the most advantageous time to institute iodine as an adjunct form of therapy. The reviewer believes that the dose of propylthiouracil is 100 milligrams, t.i.d., daily, and this should be continued until the basal metabolic rate is zero or less, and then reduced to 100 to 150 milligrams daily. Furthermore, it is my opinion that iodine in the form of 4 minims of Lugol's solution daily should be given from the very beginning of treatment.

It is the belief of Dr. Means that propylthiouracil will produce a remission in patients with Graves' disease which will continue as long as the drug is given without interruption. This is correct but the statement is incomplete. It has been demonstrated, for example, that after the drug has been given for as long a period as is necessary to maintain the basal metabolic rate within normal limits for ten months or more, the therapy may then be discontinued completely, and in an appreciable number of patients a long remission will follow. The preparation is, therefore, not only highly satisfactory as preoperative medication but it should also be given consideration as a form of medical treatment.

It does not appear that the author has placed sufficient emphasis upon the important differences between exophthalmic goiter and toxic adenoma. In the reviewer's opinion, they are separate diseases with some aspects in common, but with significant variations in their behavior. For example, patients with toxic adenoma are less susceptible to the action of iodine, cancer may develop as a complication, they are more readily cured surgically, serious eye complications do not appear, they less frequently develop "thyroid crises," spontaneous remissions are less frequently observed, and cardiac complications are more commonly present. References to these differences have not been entirely omitted from the discussion; they appear much more important, however, to one who has practiced medicine in an area where nodular goiter is commonly observed.

One of the debatable aspects of thyroid disease is the clinical significance of a solitary nontoxic adenoma. Widely divergent views have been expressed about the possibility of such a condition progressing to the state of malignancy. It is stated in this monograph (p. 453) that "during the past 3 years we have made it a practice to advise surgical intervention in all patients found to have single discrete nodules of the thyroid." In 199 specimens thus obtained 19 per cent had malignancy. There follows a discussion of the discrepancy between the high incidence of malignancy in surgically removed thyroid tissue as compared with the relatively low percentage of thyroid cancer observed at necropsy. The conclusion of the discussion is with the statement that "one wonders as to the accuracy of some of these histological diagnoses made on surgically removed material," a point which deserves careful consideration.

The volume contains a comprehensive bibliography bearing on thyroid disorders, and hence is exceedingly valuable as a source of references bearing on these topics. The reviewer would warmly urge that in all such monographs the references with the full title be placed at the bottom of the page on which they are cited, rather than at the end of each chapter, as they are in this volume. Furthermore, in searching for a reference by any particular author, a complete alphabetical bibliography at the end of the book is always a great convenience.

The reviewer does not wish to detract from the value of the publication by any of the criticisms which have been made. In general, the volume is made up of an exceedingly well written collection of information bearing on the subject. It should be consulted by every person desiring to obtain a comprehensive and fundamental knowledge of this field.

Cyrus C. Sturgis, M.D.

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

Department Editor: GEORGE M. WYATT, M.D., 1835 Eye St., N.W., Washington 6, D. C.

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ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

Jonsson, Gunnar. Points regarding synovial fibrosarcoma. *Acta radiol.*, 1948, *29*, 356–357.

The most important differences between synovialoma and synovial fibrosarcoma are the following:

1. Synovialomas contain endothelium-lined cavities, formations which are lacking in synovial fibrosarcomas.

2. Synovialomas often metastasize to the regional lymph nodes. Synovial fibrosarcomas do not. Both types of tumor, on the other hand, metastasize to the lungs and other distant organs.

3. Synovialomas are often highly radiosensitive while synovial fibrosarcomas are insignificantly so. In other respects there is a great resemblance between the two types of tumor even as regards prognosis. Synovialomas are considered to have a very poor prognosis. The prognosis of synovial fibrosarcomas appears to be somewhat better but even these tumors must be regarded as very serious.

Knutsson pointed out in his article the diagnostic importance of the fact that synovial fibrosarcomas often contain calcific deposits. Deposits of this kind do not occur in synovialoma or inflammation in the tendon sheaths, bursa or joint capsules. The deposits which are characteristic in appearance can be demonstrated roentgenographically and permit a correct diagnosis in most cases.—*Mary Frances Vastine.*

Hughes, E. S. R. Osgood-Schlatter's disease. *Surg., Gynec. & Obst.*, March, 1948, *86*, 323–328.

A knowledge of the normal anatomical and roentgenological features of the tibial tuberosity in the varying stages of its development is indispensable if the true nature of Osgood-Schlatter's disease is to be understood.

It seems that the pathological change in this condition is primarily within the ligamentum patellae rather than in the apophysis. The ossification at the site of insertion is readily accounted for by the partial tearing of the ligamentum from the bone.

This conception of Osgood-Schlatter's disease as a "tendinitis ossificans" is in full accordance with all the known facts. Trauma was believed by both Osgood and Schlatter to be the cause of the painful tuberosity and this opinion is now regarded as correct. The finding by some authors that the first roentgen sign of this disease is a thickening of the ligamentum patellae; the almost constant roentgenographic demonstration of opaque material within the ligament; the increase in density of this material in successive roentgenograms, all favor the view that Osgood-Schlatter's disease is of the same pathology as myositis ossifications which occurs in the muscle and tendinous fibers of the brachialis at the elbow.

With the great number of variations possible in the roentgen appearances of the normal tuberosity it is most hazardous to diagnose Osgood-Schlatter's disease from such appearances as increased densities, osteoporosis, partial separation, pitting, irregularities, and similar conditions. The appearance of fragmentation is a normal stage in the apophyseal development. Osgood-Schlatter's disease cannot be compared with osteochondritis of the hip where fragmentation is a roentgen sign of disease. The only definite abnormality of the apophysis observed here was the osteoporosis of the surface at the site of insertion of the ligamentum. This was observed clearly in only 5 cases and its presence is accounted for by a reactive hyperemia at the site of the injury.

It may be concluded that there is the strongest evidence in support of the belief that Osgood-Schlatter's disease is primarily an intraligamentous rather than an epiphyseal condition.—*Mary Frances Vastine, M.D.*

CAVE, EDWIN F. Fractures of the tibial condyles involving the knee joint. *Surg., Gynec. & Obst.*, March, 1948, *86*, 289–294.

Fractures involving the joints, especially weight-bearing joints, should be restored to normal anatomical relationship as accurately as possible, and if necessary, by surgical measures. This applies particularly to fractures of the tibial condyles involving the knee joint.

The commonest and also the fracture most difficult to handle involving the tibial condyles is the "bumper" or "fender" fracture which produces major damage to the lateral tibial table with or without damage to the external semilunar cartilage, the internal lateral ligament, and the cruciate ligaments.

Roentgen Studies. Roentgenograms of both knees should be taken in the same relative positions with anteroposterior, lateral and oblique views. If the injured knee is held in a position of flexion, the normal knee should be roentgenographed in the same position. Little knowledge is gained from the lateral views while the anteroposterior and oblique views will reveal the diagnosis. Because of the soft tissue swelling, more than the usual roentgen-ray penetration should be used to demonstrate the fracture lines.

Conclusions

1. Many fractures of the tibial condyles with more than a moderate degree of displacement should be treated by open reduction and internal fixation.

2. The surgeon undertaking such an operation must be well trained in meticulous joint surgery.

3. Preliminary manipulation and compression of many fractures of the lateral and medial tibial condyles may do harm to the joint surface of the tibia and make the subsequent open reduction more difficult.

4. Extensive comminuted fractures involving both tibial condyles may not be successfully reduced either by closed manipulation or open reduction.

These conclusions are based on a study of 98 cases of which 24 patients were treated by open reduction and internal fixation.—*Mary Frances Vastine, M.D.*

VARGA, CHARLES, RICHTER, MAURICE N., and DESANCTIS, ADOLPH G. Systemic aleukemic reticuloendotheliosis (Letterer-Siwe disease). *Am. J. Dis. Child.*, March, 1948, *75*, 376–384.

Three cases of systemic aleukemic nonlipid reticuloendotheliosis are reported. In the first case, the only change noted in roentgenograms of the long bones was moderate calcium deficiency in the cancellous portions. In the second, roentgenograms of the long bones revealed no abnormality. In the third, proliferative periosteal changes with numerous small areas of rarefaction were found in the skull and long bones. Two of the patients exhibited cutaneous manifestations not unlike infected eczema.

Roentgen therapy was not used in the treatment because, the authors state, it is not generally considered effective and, in addition, a depression of the functional acitivity of the reticuloendothelial system by irradiation with aggravation of existing infection has been noted.

A brief discussion of the relation of the condition to many better known diseases is included and difficulties in diagnosis and resistance to therapy are discussed.—*R. S. Bromer, M.D.*

KEMP, F. H., and WILSON, D. C. Some factors in the aetiology of osteochondritis of the spine. *Brit. J. Radiol.*, Oct., 1947, *20*, 410–417.

Two families in the laboring class in villages in England have been studied roentgenographically. The characteristic changes of osteochon-

dritis of the spine were found in many members of both families. In one family the parents both presented upper dorsal kyphosis with changes indicating healed osteochondritis. Children born when the family was in fair financial circumstances and obtaining a fairly good diet have normal spines. Of the children who grew up in less favorable times, several have the same type of upper dorsal scoliosis as the parents, and of these, several have changes of osteochondritis.

In the second family, the father has a lower dorsal scoliosis, and a pronounced lordosis. The family circumstances have always been poor, with some chronic minimal malnutrition. Some of the children show the same type of abnormal curvature as the father, and of these, some show osteochondritis.

The authors feel that this investigation indicates that osteochondritis develops from a combination of poor posture, which may be copied from the parents, and poor feeding. Healing takes place with improvement in the social circumstances. Although the water supply of both families contains a moderate amount of fluorine, it was not felt that there was conclusive evidence that this played a part.—*E. F. Lang, M.D.*

Watkins, W. Warner. The "last-straw" factor in low back disability. *Radiology*, Jan., 1947, *48*, 20–28.

The author reviews 100 cases of low back disability examined and evaluated by the Medical Advisory Board of the Industrial Commission of Arizona, over a nine year period. Of these 100 cases, 42 showed no visible bone or joint pathology, 33 showed definite bone or joint changes and 25 showed developmental anomaly with or without bone changes. Of the 42 cases without demonstrable roentgenologic evidence of pathology, 59.5 per cent were classified as having symptoms not attributable to injury. Of the 58 cases showing visible bone and joint changes or development anomalies, 33 cases exhibited arthritis of varying degrees.

This analysis was presented in defense of the conclusions reached by the Medical Advisory Board as a possible basis for comparison with similar ratings established by other boards. The author, a radiologist, discusses the factor of adaptation of the human body to certain disease processes, this adaptation at times being altered by sudden stresses, by processes which require unfamiliar use of certain body organs, and by the added factor of nervous exhaustion. He uses the classification of arthritis set up by the American Rheumatism Association. He feels that the chronic bone and joint changes found in the lower spine will fall into one of three groups: (1) bone changes from specific infection and neoplasm, (2) rheumatoid arthritis and (3) osteo-arthritis.

He states that pain practically always precedes the development of visible bone changes in rheumatoid arthritis but that the bone changes in osteo-arthritis precede the development of symptoms.

The question often raised in the evaluation of back injuries is the following: "When a man has a slowly developing arthritis of the spine which is being compensated for by adaptive changes in structure and mechanics, so that his working ability is not materially reduced, and some last-straw factor which would not cripple a normal back breaks this compensatory adaptation and results in disability, to what extent shall the disability be chargeable to the accident?" It is interesting that in this series of 100 cases of low-back disability, only one myelographic examination was carried out, and this demonstrated an extruded disc at the fourth lumbar interspace.

The author stresses the necessity for an intelligently directed and carefully supervised rehabilitation of workers having low-back disabilities. —*Robert C. Pendergrass, M.D.*

BLOOD AND LYMPH SYSTEM

Bazy, L., Huguier, J., Reboul, H., Laubry, P., and Aubert, J. Sur quelques aspects techniques de l'artériographie. (On some technical aspects of arteriography.) *Arch. d. mal. du coeur*, March-April, 1948, No. 3–4, pp. 97–112.

Five criteria are given for satisfactory arteriography, the most important ones being the innocuousness and the rate of injection of the opaque substance. Great care should be taken to render this rate as nearly equal to the speed of the circulation as possible, to prevent vascular dilatations or spasms. The authors criticize the previous methods of arteriography (where arterial circulation is partially or completely blocked).

The authors believe their method, which they call arteriography with free circulation, meets better the criteria. Several excellent arteriograms accompany the article. Their method

enables a kinetic study also. They use a very hypertonic solution of tenebryl 411 (680 mg. of I per 1 cc.) 100 to 110 per cent—10 to 15 cc.—which they inject into the artery very slowly under controlled pressure of about 1,000 to 1,400 grams. The authors consider that this very slow injection of a very opaque substance will prevent abrupt changes in intravascular pressure except in individuals with definite vasomotor instability. Since 1935 they have tried to eliminate such persons from arteriographic studies by two tests: (1) the reflex oculocardiac reaction, and (2) the intracutaneous reaction with adrenaline. Also they do not use arteriography in cases of hyperspasm (Raynaud's disease, ischemic syndrome of Volkman) unless the study is imperative in which case they are very cautious.

The intra-arterial pressure should be controlled every moment to avoid hypertension which is the most important danger. The authors have perfected an apparatus which enables them to measure this pressure during the injection giving thus an important margin of safety. A direct injection into the abdominal aorta gave a complete visualization of the lower extremities (serial arteriograms every five seconds).

After an extensive study of the various contrast substances for arteriography, the authors state that the ideal substance has yet to be found. At the present, they think that tenebryl 411 (an organic-iodine compound) is the best.—*J. N. Sarian, M.D.*

GENERAL

PACK, GEORGE T. Prepubertal melanoma of skin. (Editorial) *Surg., Gynec. & Obst.*, March, 1948, *86*, 374–375.

The groups of nevus cells constituting this congenitial tumor may be in evidence at birth. The coloration of these tumors, however, seems to develop after birth with exposure to light. Many of these tumors do not increase in dimension except proportionately with the rate of the growth of the child. Many of these nevi are not visible at all until after the onset of puberty. A child with a few scattered pigmented moles here and there may, in company with the endocrine changes attendant on the state of puberty, have the rather sudden development of numerous pigmented nevi over the skin of the face, trunk and extremities. It is assumed that these are not new-growths in the strict sense of the word but that the congenital misplacement of these cells may have been present but unrecognized until influenced by the hormonal factors so increased at this time. With the onset of puberty the nevi become much more darkly pigmented and have a tendency to become elevated.

There is one important type of pigmented nevus which bears such a close resemblance to malignant melanoma that it is not possible, clinically, to distinguish between the two. This nevus is found in children up to the age of puberty. Even though this tumor has structurally the conformation of the true melanoma it ordinarily does not behave as such until after puberty. The author's experience with more than 900 cases of malignant melanoma has been that none of these melanotic tumors of infancy and childhood has metastasized to regional lymph nodes although many of them have been labeled as malignant melanoma by extremely competent pathologists. He suggests that we adopt such a term as "prepubertal melanoma" to indicate the group of tumors which resemble malignant melanoma histopathologically but do not behave as such.

It would seem that the malignant melanoma in its derivation from the pigmented nevus is a tumor closely related to the endocrine system and markedly influenced by the activity of the endocrines, notably the gonads, the suprarenal cortex and the hypophysis. It is obvious that complete surgical removal of all dark deeply pigmented nevi in childhood is necessary. Their removal in infancy and childhood entails very minor surgical procedures without the hazards of recurrence.

In reviewing the end-results of the treatment of melanoma at the Memorial Hospital the number of five year survivals without recurrence (definitive cures) was only 50 per cent as good in the group of patients whose ages extended from puberty to twenty-five years as it was in the older age group.—*Mary Frances Vastine, M.D.*

REILLY, WILLIAM ANTHONY, and LINDSAY, STUART. Gargoylism (lipochondrodystrophy). *Am. J. Dis. Child.*, April, 1948, *75*, 595–607.

In this report are described the clinical, laboratory and roentgenographic manifestations seen in 16 patients with gargoylism observed during a seventeen year period. On 8 of these 16 patients autopsy was performed.

Gargoylism is a disease involving most of the tissues of the body. The skeleton is greatly

altered and may be the earliest site of clinical manifestations. The disease is usually characterized by the following signs: typical facies (like a gargoyle), resembling that of cretinism; cloudy corneas; skeletal changes in both bone and cartilage; dwarfism; infantilism; thickening of the skin and periarticular structures limiting extension of joints; hepatosplenomegaly, and mental retardation. There is occasional familial recurrence, but no predilection as to sex or race has been noted.

Observations by Tuthill at the first autopsy of the condition which was reported indicated the storage in the brain of a lipid resembling cerebrophosphatide. Other later reports of autopsies did not confirm this, but later Strauss also contended that an excess of lipid was found in the involved tissues. After a thorough search of the literature, the authors found 107 case reports up to January, 1947. The appearance of clinical signs in infants as young as two months of age (kyphosis), the familial recurrence in 5 of 13 of the families in their study and the altered skeletal growth, they think, would indicate a hereditary defect of the germ plasm. Likewise, the storage phenomenon in the tissues, possibly of the carbohydrate type, could be regarded as a constitutional metabolic disorder. They feel that there is storage of some material in the parenchymal cells of the body. This material is not lipid in nature and may be a carbohydrate. In a later paper, they will report in detail the pathologic lesions observed in their autopsies.

The paper contains discussions of the etiologic aspects, signs and symptoms, laboratory data, roentgenographic findings, diagnosis, prognosis and treatment. In roentgengrams, the skull is usually dolichocephalic and the frontal areas overlie the orbits anteriorly to a considerable degree. The sella turcica is elongated and is shallow. The clinoid processes are often poorly developed and stand upright and are not eroded. The maxilla and, in many patients, the ascending mandibular rami are underdeveloped. There is forward protrusion of the mandible with an overbite of the lower incisor teeth.

The scapulas, in many patients, are widened. The ribs have narrow roots and broad bodies, with necks which appear distorted. The clavicles are distorted and wide. The superior halves of some of the vertebral bodies (between the 12th thoracic and the 2nd lumbar level) do not ossify at the same rate as the inferior halves, so that there is a steplike formation in the anterior surfaces of these bodies, resulting in the kyphosis so often noted clinically.

In the extremities the magnitude of the changes varies greatly but they are more pronounced in the upper than in the lower extremities, and the upper extremities are invariably affected. There is decided retardation of epiphyseal maturation, with abnormal configuration of the shafts and irregular cartilaginous proliferation at the epiphyses. The shafts are short and stubby and exhibit bizarre swellings in the central portions which taper toward the ends. Reilly and Lindsay regard this as a significant diagnostic sign. The head of the humerus is thick and often has a valgus angulation. The articular surfaces and the epiphyseal plates of the lower ends of the radius and ulna face inward. The metacarpal bones, the proximal portions of the metatarsal bones and the phalanges are broadened and shortened, and the first two phalangeal bones are pointed at their ends. Both acetabulums are shallow, and the ischia are disproportionately small in relation to the ilia. The femurs show a coxa valga angulation of the neck and a malformed, flat appearance of the head. The necks are broad. Invariably genu valgum is present. Occasionally, there is a fragmentation in the ossification process and the epiphyseal plates often have irregular outlines of ossification.

The differential diagnosis from Morquio's disease is discussed in the section on diagnosis. The authors question whether Morquio's disease is essentially the skeletal form of gargoylism as their roentgenologic appearances are so similar. To date, there have been few adequate descriptions of the pathologic features of Morquio's disease. In a biopsy report of Shelling, the changes in Morquio's disease in the bones were similar to the osseous lesions found by the authors in gargoylism.

In the treatment of the condition, endocrine products are of no great value. Symptomatic therapy is indicated even if given only as a placebo. Families should be warned that the disease not infrequently may recur in future offspring.—*R. S. Bromer, M.D.*

ROENTGEN AND RADIUM THERAPY

Eberhard, Theodore P. Treatment of epitheliomas of the skin. *Radiology*, November, 1947, *49*, 620–626.

The author gives a plan of treatment for basal, squamous, and basosquamous cell epi-

theliomas of the skin which disregards histology as a criterion for choice of method. Biopsy is always taken so that the lesion is definitely established as belonging to the epithelioma group. The method of treatment depends primarily on the size and location of the lesion, and secondarily upon the anticipated cosmetic result. The size and location will often determine the relative advantages of radium, roentgen radiation and surgery. Voltages used in roentgen treatment varied from 120 to 140 kv. Daily doses of 300 and 400 r were first used, but better cosmetic results were obtained with smaller initial doses. The first 1,600 r were then given at the rate of 200 r per day, the next 1,200 r at 300 r per day and the next 800 r at 400 r per day. The total doses were aimed at getting at least 300 tissue roentgens into the depth of the tumor.

Statistics are given regarding 492 patients treated in three years. At the end of a three-year follow-up period, 327 patients (66.4 per cent) were living free of disease and 89 (18.1 per cent) had died of other diseases. With Magnusson's correction factor, the cure rate is 83.3 per cent. No significant differences are observed in the results from the three types of treatment.—*J. Paul Bennett, M.D.*

Dewulf, L. Le traitement de l'epithelioma des paupieres. (Treatment of epithelioma of the eyelids.) *J. belge de radiol.*, May, 1947, *30*, 255–264.

The author reviewed 76 cases of epithelioma of the eyelids treated by contact roentgen therapy. He lists the indications and contraindications of this form of treatment, and states why this treatment is preferred over radium therapy. The indications are as follows:

1. Technically the method of application is easier.
2. The roentgen-ray beam can be directed in such a way that the eye will receive a minimum amount of radiation.
3. The treatment can be made while the patient is ambulatory.
4. Contact roentgen therapy by the fractional method gives an almost invisible cicatrix.—*Panagiotis S. Nemfakos, M.D.*

Jacobsson, Folke. The treatment of keloids at Radiumhemmet. *Acta radiol.*, 1948, *29*, 251–267.

At Radiumhemmet 625 cases of keloids have been treated during 1921–1941. In 112 cases the keloid had earlier been excised surgically one or more times with subsequent recurrence. Five hundred and forty-nine cases were treated with radium, 24 with radium and roentgen rays and 25 exclusively with roentgen rays. The keloid was excised in 27 cases and then within ten days the scar was prophylactically irradiated. Total regression of the keloid was obtained in 73.6 per cent of cases, considerable regression in 14.4 per cent, evident in 9 per cent, slight regression in 1.9 per cent and the result was unsatisfactory in 1.1 per cent.

A keloid ought to be treated with radium before it is more than one year old because it then becomes less radiosensitive. The best results are obtained in keloids caused by mechanical injury or operation and the poorest in keloids in the sternal region and in cases with more than one keloid and different causes. In the latter cases irradiation should be given prophylactically to every significant lesion of the skin.

Since 1936, the author has used radium in applicators as advised by Strandqvist. The dose is calculated as the number of roentgens delivered in a 1 centimeter tissue layer. The dosage varies between 600 and 1,200 r. A dose of 900 r, for example, is delivered in two hours by an applicator containing ten needles (100 mg. radium) arranged in one row.

A careful dose must be given to keloids caused by burns. Skin tolerance is decreased in these keloids and there is risk of necrosis.

If there is no definite regression of the keloid after one to one and a half years and there are still pronounced symptoms such as itching and pain, a second treatment should be given. In most cases, however, one treatment will be sufficient.

In irradiating spontaneous keloids, especially those in the sternal region, a margin of at least 5 mm. of the surrounding apparently normal skin should be treated. Large keloids should be treated with roentgen irradiation because the dose will be more uniform than with a radium applicator.

The combination of operation and subsequent irradiation is not recommended, as a rule. Since the results of irradiation alone are usually as good, this method should be tried first.—*Mary Frances Vastine.*

Manjunath Rai, K. Treatment of leucoderma and the technique employed. *Indian J. Radiol.*, May, 1947, *2*, 45–50.

The author had treated 12 cases of leukoderma (using superficial roentgen therapy) with good results in all. The dosage used was not stated, but he thought that the late effects of irradiation to large areas could very possibly discourage its general use.

Ultraviolet ray therapy was then tried and a 90 per cent cure rate of those treated was obtained in 186 cases. The technique and basis of selection of cases are given in the article.—*R. Datzman, M.D.*

Lawrence, J. H., Dobson, R. L., Low-Beer, B. V. A., and Brown, B. R. Chronic myelogenous leukemia. *J.A.M.A.*, March 6, 1948, *136*, 672–677.

Since P^{32} emits beta rays whose half-value layer of tissue is about 2 mm., it was thought this would be an excellent way to give localized irradiation to the marrow.

Calculations revealed that 1 microcurie per gram of tissue will give a total of approximately 40 r of body irradiation in a twenty-four hour period.

The usual doses given were 1–2 millicuries one to two times weekly for four to eight weeks but doses equivalent to 40 millicuries intravenously over a period of seventy-two days have been given.

One hundred twenty-nine patients with chronic myelogenous leukemia were studied. With individual variations, they were given the approximate dosage listed above in an attempt to bring about clinical and hematologic improvement without damaging the normal cells.

It was noted that prophylactic or preventive treatment was ineffective. In this group ordinarily treatment was required on an average every six to nine months; occasionally one to two years elapsed however. Average length of life after onset was three to seven years.

No evidence of lengthening of the life expectancy was found. Possible advantages are the ease of providing a generalized irradiation and doing this without radiation sickness.—*R. Datzman, M.D.*

Bogart, Franklin B., and Imler, Allison E. Giant-cell tumors of bone. *Radiology*, October, 1947, *49*, 432–440.

Most giant cell tumors of bone are benign, but there is evidence to indicate that a few are either malignant from the outset or eventually become malignant. There are a number of variants of the true giant cell tumor which, for clinical purposes, are considered giant cell tumors and are so treated. A biopsy of the tumor should be done, and there are usually no contraindications to biopsy unless the lesion is surgically inaccessible. Where the tumor is proved to be of the malignant type, it should be treated surgically. If the lesion is accessible, it should be entirely removed.

Tumors which appear clinically, microscopically, and roentgenographically to be benign may be successfully treated by irradiation. It is recognized that where they can be readily approached, they can also be successfully treated by surgical removal. In most cases it is not necessary to combine surgery and irradiation. In structures such as the spine, it seems to be a disadvantage to use curettage, since the surgery may weaken the bone where the tumor is located in a weight-bearing area. Irradiation alone produces calcification, which lends support to the involved area and results in an earlier cure.

Many have observed that cases previously treated by curettement do not subsequently respond satisfactorily to roentgen therapy. Hence, lesions which have recurred following surgical removal are believed to be best handled by surgery if the proper surgical approach can be attained.

The authors do not believe that the roentgen dosage at present advocated for children—a series of approximately 100 to 200 r delivered to the tumor and repeated at intervals of one to three months for two to four series—will cause epiphyseal damage. In some cases they have used much larger doses where growing epiphyses were not involved, giving as high a tumor dose as 1,500 r, with a second series of half that amount two months later. Experience indicates that the smaller doses are adequate. The authors agree with the previously expressed opinion that where no damage results to the skin and soft tissues, no damage will result to the epiphyses.

Four cases are described in detail, 3 in the spine and 1 in the proximal end of the tibia. All showed a satisfactory response to treatment. Three were treated by irradiation alone, and one by combining surgery and irradiation.—*Paul R. Dirkse, M.D.*

Denier, Andre. Traitement de la fievre de malte par la teleoroentgenotherapie totale. (Treatment of brucellosis by total teleroent-

gen therapy.) *J. belge de radiol.*, May, 1947, *30*, 265–271.

The author presents 17 cases, and his observations concerning his investigations. All his cases were of several weeks' and sometimes months' duration. These cases had previously received all the therapeutic methods including vaccine, colloidal metals, and sulfa drugs.

All the patients had positive serological tests. Sweating and weight loss were constant. After the first roentgen treatment there was a fall of the temperature by the second day. The factors used were as follows: 30–40 r according to the body structure of the individual, filter 1 mm. copper plus 2 mm. aluminum, 340 kv., distance 2 m. 60 cm.; position: the patient was lying on a stretcher and irradiation was applied to the entire body. The author always treats first the anterior surface and after that the posterior surface. A second dose was repeated after eight days and sometimes a third dose was necessary but this was not the rule.—*Panagiotis S. Nemfakos, M.D.*

WASSON, W. WALTER, and GREENING, ROY. Further observations with intravaginal roentgen therapy of cancer of the female pelvis. *Radiology*, October, 1947, *49*, 452–461.

The authors state the purpose of this paper is to discuss, not the successes, but rather the failures of transvaginal roentgen therapy, and to offer certain procedures with the hope of better end results. They stress the necessity for careful diagnosis and for careful selection of the treatment of choice.

In the average case 2,500 r is delivered to the structures of the birth canal by external irradiation. Since 4,000 r within the tumor cells is probably the optimal amount, there remains 1,500 r to be delivered, either by radium or intravaginal roentgen therapy. For intravaginal roentgen therapy 140 or 200 kv. is used. Care must be exercised in placing the cones so as to avoid overlapping of the areas and the production of delayed reaction and lack of uniformity of irradiation about the pelvic structures.

If a large vaginal cone 3 or 3.5 cm. in diameter is used, the radiation will cover the transverse diameter of the pelvis, provided that three areas are given in the transverse diameter. If smaller cones are used there will be a space between the areas treated which will receive very little radiation. In such a case radium may be given within the uterus, and the intravaginal radiation should then be limited to the cervix and to the nodes along the outer pelvic wall. The author recommends intracavitary radium in all second, third and fourth stages to complement the external and intravaginal roentgen therapy, particularly when the intravaginal cone is not large enough to deliver an adequate uniform dose throughout the pelvic canal. Because of delayed reaction about the cervix and vaginal vault, it is recommended that if a tumor dose of 5,000 r is given in one series it should not be repeated, at least in that amount.

Intravaginal roentgen therapy is also suggested for residual tumors following operation upon the uterus and ovaries, or about the cecum, bladder and rectum.

Another technique is offered when the intracavitary radium application is desired. By using modified bladder retention catheter, the radium may be placed inside the catheter and inserted into the urinary bladder. The radium is then inflated to the desired extent, which may be recorded and controlled by a manometer. This gives greater depth and uniformity of dosage which has been sought for some time in the treatment of tumors of the bladder and other structures.—*Gordon J. Culver, M.D.*

BOWING, HARRY H. Intracavitary radium therapy for carcinoma of the uterine cervix. *Radiology*, October, 1947, *49*, 406–410.

A method of intracavitary radium therapy is presented. All applications are made with the patient in the knee chest position. Individualization of each patient is stressed. Roentgen therapy is started a few days before radium therapy is completed.

Results are presented. From 1919 through 1929 the percentage of three year cures steadily increased. This was attributed to several factors including (*a*) a satisfactory method of vaginal endoscopy facilitating placement of the applicator and gauze packing with minimal trauma, (*b*) observation of the vaginal field during the initial days of therapy to guide the selection of treatment, (*c*) better distribution of the radium applicators, (d) early recognition and treatment of potential and actual complications, such as bleeding and serious hemorrhage, localized inflammation, and necrosis of tissue.—*J. Maxey Dell, Jr., M.D.*

WATERMAN, GEORGE W. Interstitial radium therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 411–412.

A method is presented using parametrial radium element needles. In addition a platinum capsule of 20 mg. content that will deliver into the cervico-uterine canal approximately 3,300 milligram-hours over a period of seven days is used. Adaptability of this method to all types and conditions of cancer of the cervix is stated. In the last 198 cases their absolute five year survival rate was 38.9 per cent. The method of implanting the needles is described. Sepsis, fistula formation and intestinal injury have not been in excess of such complications reported by others using different methods.—*J. Maxey Dell, Jr., M.D.*

DEL REGATO, J. A. Transvaginal roentgen therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 413–414.

The importance of external roentgen therapy is emphasized. External therapy should logically precede the internal phase of the treatment. A method of transvaginal roentgen therapy is presented. This has the advantage of completing the external irradiation without trauma to the healing tissues and without infectious complications which so often hamper the practice of intracavitary curietherapy.

A 42 per cent three year survival rate in 52 consecutive, unselected patients is reported.—*J. Maxey Dell, Jr., M.D.*

JENKINSON, E. L., PIRKEY, E. L., and HAMERNIK, J. F. Five-year end-results in the treatment of carcinoma of the uterine cervix. *Radiology*, October, 1947, *49*, 415–418.

Seventy-five cases followed out of 98 cases showed a five year survival rate of 30.6 per cent. Their treatment methods used in this series are presented.—*J. Maxey Dell, Jr., M.D.*

ERNST, EDWIN C. Improved methods of intravaginal roentgen and radium therapy in carcinoma of the cervix. *Radiology*, October, 1947, *49*, 425–428.

Two types of expanding colpostats for radium therapy in carcinoma of the cervix are described and illustrated. More accurate and uniform irradiation of the cervix, parametria and vaginal wall is claimed. Areas of tissue necrosis have not been observed in a single case. The instruments are stated to be very adaptable to the different forms of distant parametrial involvement and vaginal vault extension. A roentgenographic check of the position of the colpostat in 29 cases of moderately advanced cancer of the cervix did not disclose any displacement or shifting of the radium capsules. The ease of introduction facilitates the fractionation of radium treatment when desirable and reduces the amount of radiation exposure to the operator.

Translucent, plastic, intravaginal cones for roentgen therapy are described. These are stated to be adaptable to the various forms of vaginal canals.

Short auxiliary metallic cones of appropriate length are inserted into the plastic cones and the roentgen beam directed through the cone.

Final evaluation of the clinical effectiveness of these methods is deferred for later communications.—*J. Maxey Dell, Jr., M.D.*

FRIEDENWALD, JONAS S., BUSCHKE, WILHELM, and MOSES, SYLVIA G. Comparison of the effects of mustard, ultraviolet and x-radiation, and colchicine on the cornea. *Bull. Johns Hopkins Hosp.*, Feb., 1948, *82*, 312–325.

Similarity between the tissue reactions to the mustards with those following roentgen-ray and ultraviolet irradiation has been noted. Colchicine has somewhat similar actions. These agents produce erythema, vesication and ulceration of the skin. Visceral lesions following systemic administration of the mustards are similar in nature to those produced by deep roentgen therapy. This experimental study shows the similarity and differences of action of these agents on the beef and rat corneas. The dosages and time factors as well as the methods of application are discussed. Inhibition of mitosis was caused. Inhibition by roentgen irradiation was prompt whereas inhibition by ultraviolet and mustard developed slowly. Inhibitions of equal duration were less complete with ultraviolet and mustard than with roentgen rays. Recovery from the inhibition followed similar curves in all, but excessive mitotic activity following recovery was noted with ultraviolet and mustard but not with roentgen rays. Colchicine did not inhibit the onset of mitosis but stopped the process in metaphase. Nuclear fragmentation of the corneal cells was produced by ultraviolet, mustard and colchicine but not by roentgen

rays. Loosening of the corneal epithelium was produced by all four agents. An increase in extractable non-protein nitrogen in the cornea was found after exposure to ultraviolet and mustard but not to colchicine. The correlation of these reactions above to each other as well as the difference in mechanisms of action involved is speculated upon. Various other influencing factors are also discussed.—*Jerome J. Wiesner, M.D.*

GUZMAN, LEONARDO. Cancer of the prostate. *Radiology*, August, 1947, *49*, 214–222.

This is a plea for radiation therapy of cancer of the prostate in addition to any surgery and endocrine therapy which may be used. The author recommends implantation of radium needles into the local tumor plus external irradiation of all tumor, testes, adrenals and pituitary. His experience with 25 patients so treated indicates that good palliation may be expected, and occasionally a patient will survive a very long time. The original paper should be consulted for technical details of the radiation therapy. (While the reviewer agrees that the pain of bone metastases may be controlled by roentgen therapy, and the local tumor inhibited by interstitial radium, there is no sound experimental or clinical data which indicate that normal androgen producing cells can be influenced by the amount of radiation therapy recommended in this paper.)—*Robert P. Barden, M.D.*

PERRY, T. Sarcoma of the uterus. *New England J. Med.*, June 3, 1948, *238*, 793–799.

Eighteen cases of sarcoma of the uterus seen in the last eighteen years at the Rhode Island Hospital are presented. Leiomyosarcomas were the commonest, varying from recurrent fibroids of low malignancy to anaplastic, rapidly disseminating tumors. Round cell or stromal cell endometrial malignancies made up another large group. Several pleomorphic mixed tumors, including 3 carcinosarcomas, were seen. An infant with sarcoma botryoides, an extremely malignant tumor of the cervical portio of infants, growing in characteristic grapelike masses, was studied. Several giant cell sarcomas, of uncertain cellular origin, were included in the series.

At operation, tumor spread was usually extensive. Survival for more than a few years without recurrence was limited to those few patients who had small localized tumors showing few metastases histopathologically. Eight patients received preoperative or postoperative radiation therapy, with important irradiation response in only 2 cases. The first was a seventy year old woman with a small carcinosarcoma which became completely necrotic after 2,450 mg-hr. of preoperative intrauterine radium, without recurrence after five years. In the second, a large carcinosarcoma showed extensive but incomplete necrosis after preoperative treatment with 2,190 r to each of three fields.

Of incidental interest is the observation that 2 of the mixed cell sarcomas developed in women who had had intrauterine radium for menopausal bleeding six and ten years previously.—*Henry P. Brean, M.D.*

NOLAN, JAMES F., and STANBRO, WILLIAM. Dosage calculations for various plans of intravaginal therapy. *Radiology*, Oct., 1947, *48*, 462–475.

The practical limitations of intravaginal therapy are discussed at some length. Twelve theoretical methods of intravaginal roentgen therapy are presented, and the distribution of radiation calculated from published depth dose data. To compare the plans, the number of roentgens reaching the midline at the level of the internal and external os, and at points 2 and 4 cm. lateral to the midline and 2 cm. in an anteroposterior direction from the midline were calculated. The variations in the method of treatment for one, two and three field techniques were: changes in quality (half-value layer); alterations in size of a beam; changes in direction of the beam of radiation; dose applied per field, as well as total vaginal dose.

The first four plans utilize one field centered on the cervix. Because of the danger of necrosis in one field treatment plans with circular transparent cones, doses are limited to a dosage level of 8,000 to 10,000 r in air, and the area of effective irradiation extends for about 3 cm. from the midline at the level of the internal os.

The next four plans are presented to show the effects when high voltage radiations are sacrificed to achieve greater angulation of the beam by lateral direction of the cone. Different qualities of radiation are compared, the total dose delivered kept at 6,000 r or 12,000 r per field; 12,000 r is too much for softer types of radiation, as fairly wide areas of probable necrosis are indicated. However, radiations of 0.5 mm.

Cu half-value layer (140 kv., 25 mm. Cu filter) yield no area of necrosis.

Plans 9 to 12 utilize one straight cone and two angulated cones, the quality, dose and angulation kept constant, but the size and position of the cones varies. Three cones 3 cm. in diameter, with the lateral one angulated at the mid-point of the cervix, resulted in too much overlapping. A large central cone (4 cm. in diameter) with lateral one 2 cm. in diameter, placed in the fornices and angulated at the lateral edge of the cervix, did not yield very effective radiation at the level of the internal os. With a large central cone 4 cm. in diameter and two lateral cones 3 cm. in diameter, a more effective spread of radiation could be achieved with 6,000 r delivered by the lateral cones.

The authors conclude that: (1) the one field treatment plan is limited by the reaction to irradiation at the level of the external os, and does not control cancer in the lateral parametria. They believe it could well be used at a lower dosage as a preliminary to radium implantation, and in cases of carcinoma of the cervical stump where radium implantation is diffcult; (2) the two field method is inadequate for control of tumor cells confined to the cervix itself. The combination of intracervical tandem and interstitial needles might well complement the two field method; (3) the radiation distribution for the three field method of treatment would seem as effective as that obtained from intracavitary or interstitial radium. Intravaginal roentgen treatment carried to its maximum could be used without radium. (4) The authors expect from such procedures an improvement in clinical results.—*Gordon J. Culver, M.D.*

Neary, G. J. Physical aspects of intracavitary radium treatment of carcinoma of the cervix uteri. Part III. A New Applicator. *Brit. J. Radiol.*, Nov., 1947, *20*, 454–469.

In a previously published analytical treatment of the problem, the factors influencing the dose distribution in intracavitary radium treatment of carcinoma of the cervix uteri were investigated. It was concluded: that little fundamental improvement in the distribution of the radiation dose by modification of the basic Paris or Stockholm techniques is to be expected; that radium in the vagina should be concentrated in the midline; that the only way to increase the dose near the lateral pelvic wall is to increase greatly the quantity of radium in the vagina; and that this necessitates the use of heavy metal absorbing screens for protection of the rectum as well as other midline structures.

An ingenious applicator has been designed which uses 70 milligrams of radium in the uterus and two units of 140 mg. each in the vagina. The treatment time is seventy-two hours. The distribution of the radiation depends upon an arrangement of massive platinum filters. An important factor is the separation of the two portions of the vaginal radium by a heavy wall of platinum. This markedly reduces the dose to the vaginal mucosa and does not materially reduce the dose to the parametria. The entire lower half of the applicator is a heavy platinum filter for the rectum. Other specially shaped screens are incorporated into the applicator to control the dosage to the various portions of the pelvis. The uterine portion of the applicator is firmly fixed to the vaginal part and the latter is large enough to fill the upper vagina. The applicator weighs about 2¼ pounds. It is held in place by its firm fixation to a harness which is fixed in relation to the bony pelvis. Thus the entire applicator does not change position with change in position of the patient.

Complete isodose curves are presented for this applicator. The total energy absorption for a treatment is about 13.0 megagram roentgens as compared with 9.2 megagram roentgens for a typical Stockholm treatment.

Improvements which are to be anticipated are the use of uranium as a screening material to replace platinum and greatly reduce the cost of the applicator, and the use of certain radioactive isotopes instead of radium which will permit the use of millimeters of lead instead of centimeters of platinum in the screening materials.—*E. F. Lang, M.D.*

Speert, Harold. Late recurrence of cervical carcinoma following radiation therapy. *Am. J. Obst. & Gynec.*, March, 1948, *55*, 533–537.

Recurrence of carcinoma of the cervix after irradiation almost always occurs within less than five years. The author reports 2 cases in which the recurrence took place seventeen and one-half years and nineteen and one-half years after previous irradiation to carcinoma of the cervix.

In the first case the anatomic diagnosis in a fifty-two year old woman at death was "carcinoma primary in the cervix with extension to

the fundus, bladder, rectum, ovaries, Fallopian tubes, and metastatic invasion of periaortic lymphnodes, liver, and diaphragm; ureteral obstruction, bilateral, with hydroureter and hydronephrosis." More than three-fourths of the uterus was involved by the tumor mass. Microscopic sections at death were compared with slides made seventeen and one-half years before and the two sections were completely similar in histopathologic detail. The anaplastic nature and somewhat unusual histopathologic appearance of the cells of this tumor strengthens the impression that this was a recurrent tumor and not a new carcinoma of the cervix.

The second patient died at the age of fifty-four years with the tumor involving the bladder and rectum and with a vesicovaginal fistula and a rectovaginal fistula. Nineteen and one-half years prior to this time she had been treated with radium and roentgen rays for carcinoma of the cervix following which she was free of symptoms until several years prior to death when she experienced a foul blood-tinged vaginal discharge which persisted until death. The microscopic sections from the original cervical tumor and from the tumor at death showed epidermoid carcinoma in each case. The author feels that it is more difficult in this case than in the first to definitely prove that this is a recurrent tumor rather than two separate tumors, although she was followed in the same clinic carefully for several years after the cervical tumor was originally treated and again for the last few months prior to death so that he is reasonably certain that this was a recurrent tumor.—*Wendell C. Hall, M.D.*

Bowing, Harry H., and Fricke, Robert E. Late results of radium therapy for carcinoma of the uterine cervix. *J.A.M.A.*, July 10, 1948, *137*, 935–942.

Results of all cases (2,246) treated at the Mayo Clinic for carcinoma of the cervix by radium therapy between 1915–1944 inclusive are analyzed.

Surgery has always been maintained at the Clinic; as a result, irradiation has proved to be an excellent surgical "adjunct," otherwise radium is chosen for treatment of patients in the operable, further advanced and recurring groups. Close to 60 per cent of all cases of cervical carcinoma, including those operated upon, received some combination of radium and roentgen therapy. The number of early or favorable cases in which treatment for cure may be possible is practically always low, an estimated 10 to 15 per cent of the total. This compares with a figure of 11 per cent selected for surgical intervention. Among the favorable cases referred for radium, more are found with obesity, and other constitutional diseases as well as older patients, than are to be found among those chosen for surgery.

According to age grouping the largest number reported in the fourth decade with the numbers dropping off rapidly, both younger and older. On analysis of the age groups the authors contend that the patient of forty-nine years or less has a mildly unfavorable factor influencing her five year cure rate while the patient over forty-nine years of age carries this additional favorable factor.

They have aptly summarized the League of Nations classification as to extent of the disease as follows:

Stage I	Lesions confined to the cervix.
Stage II	There is a moderate local invasion.
Stage III	There is extensive local invasion or unilateral fixation.
Stage IV	There is a massive local invasion or metastasis elsewhere.

Only 1.3 per cent of the total number are classified as Stage I, while the majority, 66 per cent, are listed as Stage III. Comparing the stage of the disease as against the mean age in years gave the interesting fact that the mean age averages slightly above or below fifty for all stages. The youngest mean age group (46.4 years) represented those who had undergone some operative procedure such as cauterization or amputation of the cervix before reporting for admission to the Clinic. In attempting to analyze the five year survival rate as compared to the age grouping, much of the authenticity is lost due to the proportionately small percentage of patients traced (varying from 25 per cent to 43.6 per cent). This difficulty is of course explained by the fact that patients after discharge scatter widely to their homes.

Study of the grade of malignancy (Broders' grouping) brings out the fact that the highest percentage of survival of "traced" patients, 57.1 per cent, are grouped as Grade 1 and the lowest, 19 per cent, represent that group which the pathologist has failed to grade for various reasons. The authors admit that radiosensitivity is more complex than the microscopic analysis of the tissue; other factors which have an

important bearing on prognosis include the blood supply to the tumor bed, as well as the judgment, skill and radium technique applied by the radiosurgeon.

The authors individualize their technique with the interval between radium application prolonged where the response to treatment is prompt and shortened where the response is prolonged. Patients with serious local complications as inflammation, ulceration, necrosis and bleeding are seen and treated almost daily. Total radium treatment time for the average Stage III patient is about three weeks. Roentgen therapy is begun on the final day of radium treatment. Two anterior and two posterior pelvic ports are outlined giving a total of 500 to 700 r per field. This roentgen irradiation cycle may be repeated after a three month interval. Follow-up consists of re-examination every three to four months for the first post-treatment year, every six months for the second post-treatment year and yearly thereafter.

The five year survival rate is modified in that those patients lost to follow-up are not included in the final figure. Interestingly enough a higher per cent of Stage II traced cases (65.3 per cent) survived five years than Stage I traced cases; this is partly accounted for by the fact that only a small number in Stage I (10) were traced for five years. Five year cures, however, occurred in all classifications. There were five deaths, a hospital mortality of 0.2 per cent. The serious morbidity rate was equally low.—*William E. Howes, M.D.*

RADIOISOTOPES

Henshaw, P. S., Riley, E. F., and Stapleton, G. E. The biologic effects of pile radiations. *Radiology*, Sept., 1947, *49*, 349–360.

Experiments were carried out with strains of mice to determine the late effects of periodic and single exposures of penetrating radiations (fast neutrons, slow neutrons, gamma rays, and beta rays). In general, the late effects of penetrating radiations consisted of generalized atrophy and neoplasia of hemopoietic organs. Neoplasia may or may not result directly from the atrophic condition.

Different thresholds of damage were found. Survival time, one of the most sensitive responses, showed effects following daily exposures in the range of 0.1 n of fast neutrons and 1 r of gamma rays. Threshold responses of the peripheral blood were often less sensitive than the threshold survival responses. Threshold levels were not determined for single exposures.

The r/n ratio of gamma rays to fast neutrons for the different effects varied roughly from 8 to 1 to 35 to 1 for the conditions and methods used.

The accumulated evidence indicates that the degree of biologic effect varies not only with the dose but also with the density of ionization produced.

The incidence of lymphoma following exposure to penetrating radiations was raised from 15 per cent in the controls to over 60 per cent in groups receiving single doses of 500 and 700 r of gamma rays.

Lung tumor incidence was increased little, if any, by the treatments given. Many types of skin carcinomas developed following sublethal doses of beta rays. It is significant that hemopoietic tissue tumors were obtained with penetrating radiation and skin tumors with surface-absorbed radiations.—*Paul R. Dirkse, M.D.*

Dougherty, E. C., and Lawrence, J. H. Isotopes in clinical and experimental medicine. *California Med.*, July, 1948, *69*, 58–73.

All of the known 96 elements exist in several nuclear forms. Of the 81 stable elements, 60 have more than one stable isotope. Over 600 unstable isotopes are known, including at least one for each of the 96 elements. Only 7 stable isotopes have found biological use, but over 70 unstable isotopes have had some biological application.

Clinical use of radium and its decay products is well known, and constitutes one type of isotope application. Artificial isotopes of phosphorus and iodine have an established therapeutic value. Others have received preliminary trial. Usefulness depends on, and is limited by, the degree of selective localization in tissues or organ systems. For example, radiophosphorus concentrates in the nucleoprotein fraction of rapidly growing tissue, radioiodine localizes selectively in the thyroid gland, and certain isotopic colloids may be largely localized in selected parts of the reticulo-endothelial system. Ideally, successful use of radioisotopes in therapy of neoplasms might include radiohydrogen or radiocarbon; the beta rays of these isotopes have a penetration range of the same order as the diameter of a neoplastic cell.

Radiophosphorus in Therapy and Diagnosis. In polycythemia vera, several years of complete

hematological and symptomatic remission may be obtained with radiophosphorus therapy. Retreatment is usually necessary within three years. In chronic leukemia, radiophosphorus appears to be as satisfactory as roentgen therapy, and it may prolong life somewhat further. It has the advantage of not producing radiation sickness, but may result in anemia, thrombocytopenia, or leukopenia. In a series of over 300 patients with chronic leukemia treated with radiophosphorus, average duration of life after onset of symptoms was almost five years, and over 30 per cent have lived over five years.

Miscellaneous applications of radiophosphorus include local application to skin lesions, and interstitial injection into tumor areas. Exploration of its diagnostic possibilities has begun with the demonstration of counter-detectable localized radioactivity in superficially located rapidly growing tumors.

Radioiodine in Therapy and Diagnosis. Oral administration of radioiodine is a simple and effective method of controlling or curing many cases of hyperthyroidism. Occasional adenocarcinomas of the thyroid with iodine-metabolizing metastases respond favorably to radioactive iodine. Radioiodine is useful in demonstrating levels of thyroid hypofunction or hyperfunction, and may be used to distinguish between simple hyperthyroidism and the ophthalmopathic type.

Other Radioisotopes in Therapy and Diagnosis. Radiosodium has been used in chronic leukemia, but lacks the selective localization of radiophosphorus. Its effects are comparable to that of total body irradiation. Radiosodium has been found useful in estimating circulatory adequacy of the extremities in certain vascular diseases.

Radiostrontium has had trials in the therapy of malignancy in bone, as its distribution in the body follows that of calcium. Radioactive colloids have shown selective localization in the reticuloendothelial system which may prove useful. Anhydrous chronic phosphate, which may be tagged with radiophosphorus, localizes almost entirely in the liver and spleen. Radioisotopes of yttrium, zirconium, columbium, and gold may, depending upon the method of preparation, concentrate in the liver and spleen, or go in equal concentration into the bone marrow. Colloidal manganese dioxide, and possibly radioactive gold as well, may be localized selectively in the lymphoid tissue. Interstitial infiltration of neoplasms with zinc or gold radioactive colloids has resulted in effective localization and in tumor regression.

Certain isotopes, such as those of lithium, boron, and fissionable isotopes such as uranium and plutonium, release large amounts of ionizing radiation upon being bombarded with slow neutrons. If such material can be localized in given tissues or tumors, and the region subjected to slow neutron bombardment, a higher radiation can be conferred on the isotope-containing tissue than on the uninvolved tissue through which the neutrons must pass. A few experimental studies of this principle, using mouse tumors, have shown the predicted enhanced effect.—*Henry P. Brean, M.D.*

KNAUSS, HAROLD P. Slide rule calculations of radioactive decay. *Science*, March 26, 1948, *107*, 324.

This article describes the use of the ordinary slide rule in making calculations on the decay of radioactive substances. Details of the use of the slide rule for this purpose are given.

LISCO, HERMANN, FINKEL, MIRIAM P., and BRUES, AUSTIN M. Carcinogenic properties of radioactive fission products and of plutonium. *Radiology*, Sept., 1947, *49*, 361–363.

An intelligent appreciation and evaluation of health hazards, whether by ingestion or inhalation or by wound contamination with small amounts of radioactive substances, is difficult without experimentation. These experiments were undertaken with this in mind, even though it was realized that it is notoriously difficult to design animal experiments which precisely duplicate the human hazards.

Radiostrontium (Sr^{89}) is largely concentrated in bone, and consequently bone tumors were readily produced. The incidence was approximately proportional to the dose, and the latent period—not less than about 200 days—increased with decreasing dose. Bone tumors were produced by doses ranging from 5.0 to 0.05 microcurie per gram, both with single and with monthly repeated injections. Radioactive yttrium (Y^{91}) and cerium (Ce^{144}) also produced sarcomas in the skeletal system, primarily in the long bones. Plutonium (Pu^{239}) and yttrium (YPO_4) produced local radiation damage when given subcutaneously and intramuscularly in mice. Many local fibrosarcomas were also produced at doses of 0.5 to 0.05 microgram per gram of Pu^{239} and doses of 1.5 to 0.05 micro-

curies per gram of YPO_4. Bone tumors resulted frequently in different animals injected with Pu^{239} at levels of 4.5 to 0.05 micrograms per gram, again with a latent period of about 200 days. These tumors occurred mostly in the spine, since plutonium has a greater affinity for collagenous tissue than for bone proper, while those from strontium were chiefly in the long bones.

Both plutonium and cerium showed a high concentration in the liver and frequently produced liver damage, but no true liver tumors have been seen to date. Y^{91}, which when fed by stomach tube remained longest in the colon, produced several carcinomas of the colon in rats, in the higher doses used.—*Paul R. Dirkse, M.D.*

Stanley, Malcolm M., and Astwood, E. B. The accumulation of radioactive iodide by the thyroid gland in normal and thyrotoxic subjects and the effect of thiocyanate on its discharge. *Endocrinology*, Feb., 1948, *42*, 107–123.

As others have found, thyrotoxic patients had a larger uptake of radioactive iodine in the thyroid than normal patients. After the administration of thiocyanate or ordinary iodide, the radioiodine also was more rapidly discharged. These differences, the authors feel, are great enough to provide an accurate means of detecting thyrotoxicosis.—*John W. Karr, M.D.*

MISCELLANEOUS

Best, Arthur, and Stroud, Leona. A method of x-ray reproduction of the negative x-ray film. *Am. Rev. Tuberc.*, Feb., 1947, *55*, 184–186.

The negative 14 by 17 inch roentgen film to be reproduced is placed in the cassette next to the top as opening screen of the cassette. An unexposed film is then placed next to the negative roentgen film and between it and the back screen of the cassette is placed the black protecting paper that always accompanies an unexposed film. The purposes of the black protecting paper is to prevent any fluorescence emanating from the back screen of the cassette.

The following technique is then employed: 40 inch distance, 100 milliamperes, 42 kilovolts (peak) and one-half record. The roentgen film is then developed in the usual manner. By the same technique, a negative reproduction of the positive reproduction can further be made if this is desired.—*J. J. McCort, M.D.*

Camp, John D. A grid-front cassette; a useful application of the stationary grid. *Radiology*, November, 1947, *49*, 627–628.

A method by which any make cassette can be converted to a grid-front cassette is described. The ordinary bakelite front is replaced by a metal Lysholm grid of proper size, and protected by a plastic covering. The original thickness and size of the cassette are maintained.

Use of a grid-front cassette has improved the detail of portable roentgenograms and facilitated rapid sequence exposures, where Potter-Bucky technique is slow. Extreme usefulness compensates for the rather high cost.—*George P. Keefer, M.D.*

Goldfeder, Anna. Further studies on the relation between radiation effects, cell viability, and induced resistance to malignant growth. *Radiology*, December, 1947, *49*, 724–732.

This article is number four in a series and is a comparison of effects of roentgen rays on mammary tumors autogenous to inbred strains of mice (dba and C_3H.) The tumors of both strains were diagnosed as adenocarcinoma, but they varied in clinical characteristics. The percentage of tumor "takes," the latent period (time between transplanting and the development of a measurable tumor), and the size of the tumor formation were distinctly different in the strains.

The experiments described in the article clearly show that the radiosensitivity of tumors of similar histopathological structure is variable and that the recovery process or "latent period" of similar tumor cells partially affected by irradiation is also variable. The author concludes that histopathologic classification alone is not a conclusive guide to the specification of a proper therapeutic dose for any given tumor.—*Richard E. Kinzer, M.D.*

Clark, George L. Medical, biological and industrial applications of monochromatic radiography and microradiography. *Radiology*, October, 1947, *49*, 483–495.

Roentgen-ray diffraction analysts have long made use of tubes which produce essentially monochromatic beams in contrast to the usual

polychromatic beam used in the various branches of roentgenography.

Above a certain critical voltage, different for each target element, the spectrum characteristic of the element appears superimposed on the continuous spectrum, with the result that certain wavelengths are greatly intensified. To isolate one of these characteristic intensified beams would be to produce a monochromatic beam. To accomplish this strictly requires selection and reflection by a crystal, but the very great loss of energy renders the method impractical. Less exact, but practical and in common use, is employment of a characteristic filter which cuts out all shorter wavelengths.

Production of a monochromatic beam from a tungsten target tube is impractical because the characteristic tungsten spectrum does not appear until a voltage of 69,300 has been surpassed (where the general radiation intensity is high), and because a very rare element, either lutecium or ytterbium, is required for the filter. But a molybdenum target tube will generate an intense characteristic spectrum at 20,000 volts where the general radiation is still weak and a very thin layer of a zirconium compound will serve as an effective filter. Copper, cobalt, and chromium target tubes are also practical.

The performances of a polychromatic beam produced by a tungsten target tube and a monochromatic beam produced by a molybdenum, copper, cobalt, and chromium target tubes were compared when identical voltage, focal spot sizes, focal spot-target distances, target-film distances, film, and simultaneous development were employed.

Appreciably greater definition in fine detail is produced in monochromatic roentgenograms. Examples from industry (hair-line cracks in aluminum castings), biology (pine seeds, frogs), and medicine (bones of the hand) are illustrated. Detection and demonstration of early disease may be aided by monochromatic roentgenography.

Monochromatic roentgenography is a research tool of unlimited, but as yet almost untested, potentiality, for it can be used to supplement and augment the microscope. In microroentgenography, images are registered on extremely fine-grained photographic emulsion by a monochromatic roentgen-ray beam. The technique is described and is quite simple. The images may then be enlarged up to 400 diameters. Several biological specimens are illustrated. The results obtained are striking and stimulating.—*George Cooper, Jr., M.D.*

PROSSER, C. LADD. The clinical sequence of physiological effects of ionizing radiation in animals. *Radiology*, September, 1947, *49*, 299–313.

In order that the clinical effects of irradiation be understood and methods of therapy be explored and made available, research problems in clinical physiology and biochemistry were carried out at the Metallurgical Laboratory of the University of Chicago under the Manhattan Project. The problems have been concerned with (1) ascertaining whether different kinds of ionizing radiation have similar effects upon the mammalian body; (2) measuring sensitive reactions as a function of dose, in the hope of setting permissible exposure limits; (3) searching for sensitive biological indications of exposure; (4) describing the course of radiation damage sufficiently to suggest profitable directions for research into mechanisms of such damage that might eventually lead to effective therapy. None of these objectives has been attained in a final form, but sufficient data are available to justify a summary at this time. The pattern of clinical effects of irradiation fall into the following periods: (1) initial, (2) acute, (3) subacute, (4) chronic. The effects of whole body irradiation were observed on different species of animals. Alterations were observed during the various periods in the gastrointestinal, circulatory, hemopoietic, liver, respiratory, and nervous systems.

Four generalizations can be presented on the basis of the observations made:

I. Every kind of ionizing radiation is similar in its clinical action, whether it be penetrating external radiation or internal radiation from deposited material. A similar clinical course can be observed by single and daily roentgen irradiation, and with internal radiation from deposited alpha and beta emitters (by selecting the appropriate dose, dose rate, and experimental animals). Although not studied in as great detail it appears that the clinical pattern is similar after treatment with gamma rays, fast neutrons, and slow neutrons.

II. Nearly every organ system is affected by lethal doses of every type of radiation. The most sensitive systems are the blood forming organs, the gastrointestinal tract, and the go-

nads. Peripheral circulation and heart are also affected. Terminally there may be damage to the kidneys and even to the central nervous system.

III. No single clinical reaction is peculiarly specific for irradiation damage. A similar preterminal course can be observed with toxic agents such as the nitrogen mustards; acute infections; anaphylactic shock; and various toxic chemicals, e.g., anemia in benzol and phenyl hydrazine poisoning.

IV. The clinical picture and the conditions resulting in death vary with the dose rate and the duration of exposure for both external and internal radiation. If an animal survives one depression with a given set of symptoms, it is likely to die later from a different mechanism.

A series of clinical patterns leading to death after irradiation have been identified as follows:

1. Immediate death at very high doses and dose rates with general cellular destruction.

2. Initial shock-like death seen within forty-eight hours after roentgen irradiation in some rabbits and chickens.

3. Early deaths at high doses in dogs and rats (four to six days). There is evidence of dehydration, hemoconcentration, and much gastrointestinal damage and leukopenia.

4. Acute deaths caused by irradiation from all types of ionizing radiations (except external beta rays) occur nine to twenty-one days after treatment. Severe leukopenia, extensive tissue breakdown, tendency to bleeding, high sedimentation rate, slight anemia, and altered water balance are observed. The terminal condition is one of toxemia with fever, elevated heart rate, lowered albumin and elevated globulins, high serum nonprotein nitrogen, increased serum protein, cardiovascular failure, and so forth.—*Robert K. Arbuckle, M.D.*

Barclay, A. E. Microarteriography. *Brit. J. Radiol.*, Oct., 1947, *20*, 394–404.

During an investigation of traumatic uremia in rabbits, results suggested the existence of a vascular short cut between the arteries and veins which could leave the cortex ischemic. Ordinary roentgenographic techniques failed to show any communication, and a new method was sought to demonstrate the minute vascular structures. After some preliminary experimentation, a hot cathode diffraction tube with a beryllium window was used which gave a constant beam between 5 and 50 kv. at up to 20 ma.

The rabbit kidney is injected either in vivo or after removal. Several media may be used. Thorotrast gives excellent results. Ten per cent colloidal gold or specially prepared colloidal bismuth are not only radiopaque but can also be seen in microscopic study. After injection, the kidney is fixed in the usual manner and the entire organ roentgenographed. After determination of the direction for sectioning which will give the maximum vascular pattern, sections are cut. The sections between 120 and 450 micra were most satisfactory.

Roentgenograms are made on Kodak Maximum Resolution plates. Since the sensitivity of this is much reduced when it is wet and since the sections must be kept moist with glycerine to prevent shrinkage and distortion, a thin tissue is used as a barrier between the section and the film. The most satisfactory is found to be the tissue used for the heat mounting of prints. As the sections are exposed to the air, the exposure is made as short as possible. At a distance of 8 inches, at 20 ma., and at 15 to 20 kv. a 240 micron section requires an exposure of about five minutes. If the section is thin and softer rays must be used, a shorter distance is necessary with greater distortion. The cassettes are built to fit over the end of each cone in a light-tight manner, so that the tube, section, and film are one unit. The cassette must be applied to the cone in the darkroom as there is no cover between the section and the roentgen tube, so that the maximum use is made of soft roentgen rays.

The resulting negative may be enlarged with standard apparatus and the whole section studied, but above a magnification of 10, detail is a limiting factor. On the other hand, if a small field is used a photomicrograph may be made and this in turn enlarged. This process, surprisingly, preserves the detail much better, and satisfactory magnification of 250 diameters can be obtained. This method has the disadvantage of utilizing only a very small segment of the negative.

Using this method, stereoscopic views of the entire organ were made to determine the course of the vessels, and sections were made. These were again examined stereoscopically and further sections in appropriate planes were made to show the finest vascular structures in a section 240 micra thick. Thus the picture of

the vascular supply of the organ can be built up as a whole.—*E. F. Lang, M.D.*

LOVERDO, ANDRÉ. Sur l'emploi de gants de protection radiologique chargés à l'oxyde de thorium (ThO_2). (On the use for radiological protection of gloves laden with thorium oxide.) *Compt. rend. Soc. de biol.*, June, 1948, *142*, 843–844.

Rubber gloves into which thorium oxide has been incorporated—average thickness of 0.5 gm/sq. cm.—has been tested for radioactivity with a G-M scaler. The following ionizing energies (as absorbed per gram of tissue in contact with the glove) have been computed: (a) 0.011 r.e.p. per hour due to the beta and gamma radiations, (b) 1.38 r.e.p. per hour due to alpha radiation. These figures have already been corrected for self-absorption and angular distribution and represent the average as to the depth effect. The quantity of beta and gamma radiations would fall within the limits of the American norm of radiological safety dose (supposing that the gloves are worn intermittently) but that of alpha radiation is definitely beyond the safety limit, especially for the superficial 0.1 mm. of the epidermis (which includes the layer of Malpighi). The author advises the use of a supplementary rubber glove to absorb the alpha radiation. He asks for such a modification in the fabrication of the gloves.—*J. N. Sarian, M.D.*

BARRON, E. S. GUZMAN; BARTLETT, GRANT R., and MILLER, ZELMA B. The effect of nitrogen mustards on enzymes and tissue metabolism. I and II. *J. Exper. Med.*, June, 1948, *87*, 489–520.

I. *The Effect on Enzymes.* The halogenated alkylamines ("nitrogen mustards") have certain biological properties similar to those of the roentgen ray: injury to bone marrow and lymphoid tissues, inhibition of mitosis, and production of mutants which have been the basis for their use in treatment of blood dyscrasias. When placed in neutral aqueous solution, these substances form ethylenimonium-ring compounds which are structurally similar to choline and acetylcholine, and evidence is presented indicating that they function as structural inhibitors of these enzymes, uniting with their protein portions at the side chains where combination with choline and acetylcholine usually occurs. Tiosulfate breaks down the ethylenimonium derivatives, and its presence prevents this inhibiting activity.

Nitrogen mustards also react rapidly with —SH (sulfhydryl) groups of many intermediate products of both protein and carbohydrate metabolism, some of which are essential to enzyme activity, and thus one might expect a large number of enzyme systems to be inhibited by them, but in vitro experiments do not bear this out, showing only the choline ozidase, acetylcholine esterase, and pyruvate ozidase systems to be inhibited in concentration under 10^{-3}M ($10 \times LD_{50}$). This structural inhibition is quite specific and is irreversible.

A list of the enzyme systems inhibited by these substances is given.

II. *The Effect on Tissue Metabolism.* As studied in metabolism of tissue slices and of leukocytes, and in tissues of treated animals, tissue respiration is strongly inhibited and tissue glycolysis is very little affected by nitrogen mustards. Pyruvate metabolism is profoundly inhibited. Certain oxidative and biological synthesis processes are listed as showing distinct inhibition which can readily promote cell destruction and depress the formation of new cells.

Choline was found to protect marrow cells from the respiratory inhibiting effect of nitrogen mustards, and possible development of a method to avoid toxic marrow effects by use of such a substance in treatment is suggested.

The authors propose the explanation of mitosis inhibition by nitrogen mustards, sulfur mustards, and roentgen rays on the basis of a process controlled by a sulfhydryl enzyme with very labile and reactive —SH groups, alkylated by the mustard compounds and oxidized as a result of irradiation.—*Joseph B. Stull, M.D.*

FREED, JOHN H., FARRIS, EDMUND J., MURPHY, DOUGLAS P., and PENDERGRASS, EUGENE P. Effect of low dosage roentgen radiation on the gonadotropic function of the hypophysis of the mature and immature female albino rat. *J. Clin. Endocrinol.*, June, 1948, *8*, 461–481.

A review of the literature on treatment and results of low voltage roentgen therapy in the treatment of functional menstrual disorders and sterility convinced the authors that its mode of action is still poorly understood. They note that many theories have been proposed to

explain the good results reported clinically in hypofunctional endocrine conditions and that these may be divided into two groups: (1) stimulation; (2) selective destructive action. From a survey of the experimental literature they conclude that low voltage radiation of the pituitary, with doses of 400 r (air) or less, has shown no histological effects on the sexual systems of animals. Furthermore, that the immediate and latent effects were seldom carefully observed. In view of the importance of this highly controversial problem they felt that further investigation was necessary using methods designed chiefly to evaluate the physiological effects.

From their experiments the authors draw the following conclusions:

1. Low dosage radiation of the pituitary can produce a transient effect on the normal pituitary function of the rat. Though the immediate physiological effect is in the nature of a stimulus such an effect is only transient and not prolonged.

2. Irradiation of the pituitary in small doses has no effect on the normal development of the sexual system of immature twenty-eight day old female rats.

3. There is no evidence that roentgen irradiation can stimulate living cells, if by stimulation is meant a continued acceleration of their normal growth or function.

4. Irradiation of the pituitary in small doses has no evident harmful effect in the experimental rat.—*Charles G. Stetson, M.D.*

Holmes, Barbara E. The inhibition of ribo- and thymo-nucleic acid synthesis in tumor tissue by irradiation with x-rays. *Brit. J. Radiol.*, Nov., 1947, *20*, 450–453.

In similar rat sarcomas from the same source, the content of ribo- and thymo-nucelic acid is surprisingly constant. A number of rats with a given rat sarcoma was treated after injection of radioactive phosphorus (P^{32}), and the amount of the nucleic acids determined by the amount of this substance present. It was found that the formation of thymo-nucleic acid was markedly decreased by irradiation when compared with the control group of tumors. The same effect was produced in ribo-nucleic acid but to a less marked degree. Nembutal also was found to inhibit the activity in formation of both ribo- and thymo-nucleic acids.—*E. F. Lang, M.D.*

Allen, J. Garrott; Sanderson, Margaret; Milham, Mary; Kirschon, Alice, and Jacobson, L. O. An anticoagulant in the blood of dogs with hemorrhagic tendency after total body exposure to roentgen rays. *J. Exper. Med.*, Jan., 1948, *87*, 71–86.

In times past the hemorrhagic state which along with infection is one of the most important pathological changes following large doses of radiation, has been attributed to the associated thrombocytopenia, but from the experimental evidence described in this report a substance similar to heparin is indicated. It can be biologically inactivated by intravenous protamine sulfate or by toludine blue which restore the clotting time to normal although it had been prolonged to four days in spite of normal platelets, fibrinogen, prothrombin and calcium and the administration of vitamin K.

The presence of this anticoagulant (heparin-like) substance may be demonstrated several days before other evidence of disease and before the development of the eventual thrombocytopenia. It also causes a gel formation that is quite easily broken down by shaking (this same phenomenon occurs in heparinized blood).

Attempts to isolate heparin were unsuccessful but this is not surprising in view of the very inefficient methods available which yield only a 5 to 15 per cent recovery of a known heparin sodium acid salt.

In this experiment 25 dogs were irradiated with 200 kv. roentgen rays, receiving in one dose to entire body, 450 r (0.5 mm. Cu plus 1 mm. Al filtration; 15 ma., dosage rate 6 r/min. in air at a distance corresponding to the center of the animal's body).—*Joseph B. Stull, M.D.*

Bloom, William. Histological changes following radiation exposures. *Radiology*, Sept., 1947, *49*, 344–348.

A large series of animals were exposed to a variety of internal and external sources of radiation, including roentgen rays, fast and slow neutrons, gamma rays, beta rays, and internally administered radium, plutonium, sodium,^{24} phosphorus,^{32} barium,^{140} lathanum,^{140} strontium,^{89} zirconium, yttrium,^{91} and radiocerium.

Animals were given LD50/30-days dose and fractions thereof in the hope of finding the lower limit of irradiation damage as shown by the microscope.

Irrespective of the particular external sources, the author was unable to tell which type of radiation had been used on the animals, except for external beta rays since the changes were practically limited to the skin with that source. After the injection of radioactive material, the damage qualitatively was the same with all of the materials, and the same results were produced as by the external irradiations, modified only by (a) whether the materials reached a particular organ and (b) the type of particle emitted by the radioactive isotope. The differences are due to focalization.

In general, no histopathologic evidence was found for the cause of death. That is, no differences could be seen between the animals which died with an LD50/30-days dose and those which did not die after the same dose. The author was impressed by waves of destruction in some of the animals that received high doses, so that one could speculate on somatic mutations but there was no evidence on this point.

In general a particular organ showed histopathologic changes reflecting the amount of radiation rather than species, although one animal will tolerate much higher doses than another.

With both total body external irradiation and with internal sources of radiation no evidence whatever of any primary stimulating effect of small doses was obtained. Either a damaging effect was found or no difference from the control animals.

Striking exceptions were also found to the theory that the more primitive the cell, the more susceptible it is to radiation. A more interesting part of the problem has been the general question of why certain strains of cells are sensitive and others very resistant. After more than three years' association with this project, the author has not even a clue on which to speculate. No relation to mitotic activity was found.

Evidence was found on the question of the sensitivity of the erythroblasts. In the material used, these were exceedingly sensitive to radiation, about as sensitive as the lymphocytes.—*Paul R. Dirkes, M.D.*

Fredericq, J., and Chèvremont, M. Etude histologique et histochimique de la peau de cobaye traitée par les rayons X. (Histological and histochemical study of the skin of guinea pig treated with roentgen rays.) *Comp. rend. Soc. de biol.*, June, 1948, *142*, 850–853.

After a short historical introduction, the authors state that they were interested in the sulphydril group histochemical changes in the irradiated epidermis as this group is of importance in the keratinization processes. The skin of the hind paws of some 11 guinea pigs were irradiated with single doses of 3,000 r per paw (10 were irradiated with either 1,500 r or 2,000 r, the results obtained being almost the same in all 21.) The factors of irradiation are not given (except for 1 mm. Al filtration and target skin distance of 33 cm.)

After a very marked thinning and destruction, the epidermis begins to regenerate from the borders of the lesion and soon attains a thickness exceeding greatly that of the non-irradiated skin. However it is of an abnormal appearance. The histochemical studies reveal a considerable decrease in the —SH (—Sulphydril) groups at the irradiated regions. Later on, as the regeneration starts, there is a great increase. This initial decrease does not seem to be due to a direct action of the roentgen rays on the —SH groups. In the non-irradiated parts of the skin of these experimental animals, there is elicited a temporary diminution of —SH groups.—*J. N. Sarian, M.D.*

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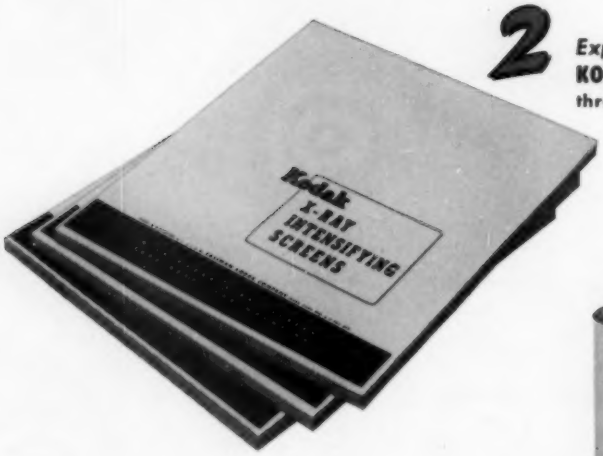

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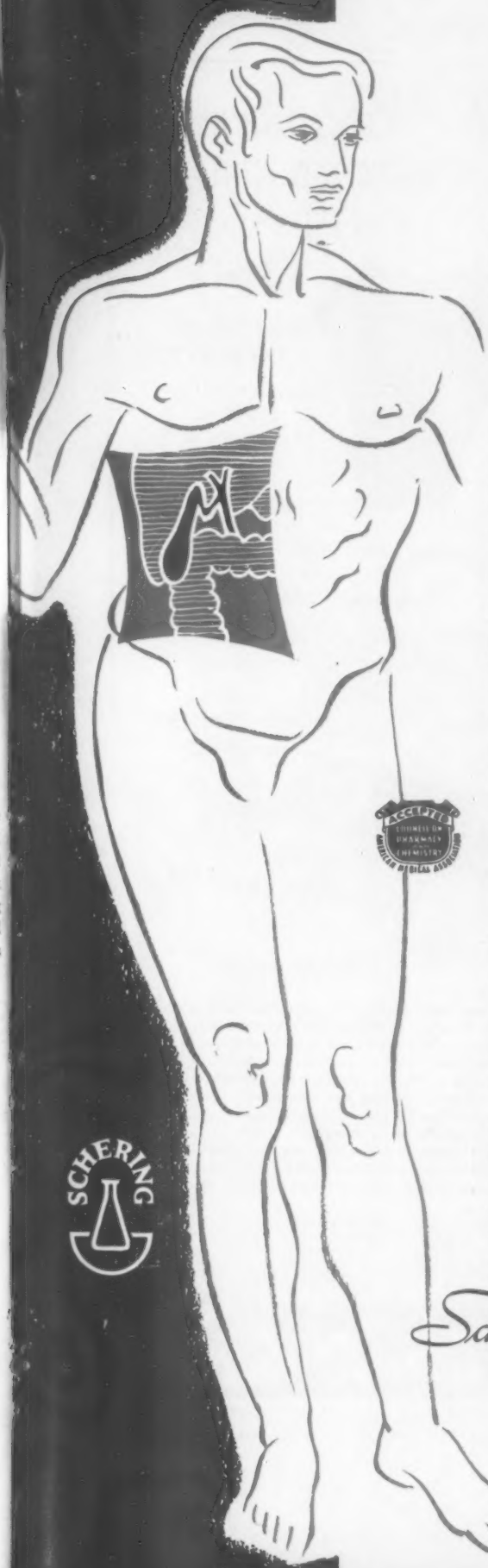

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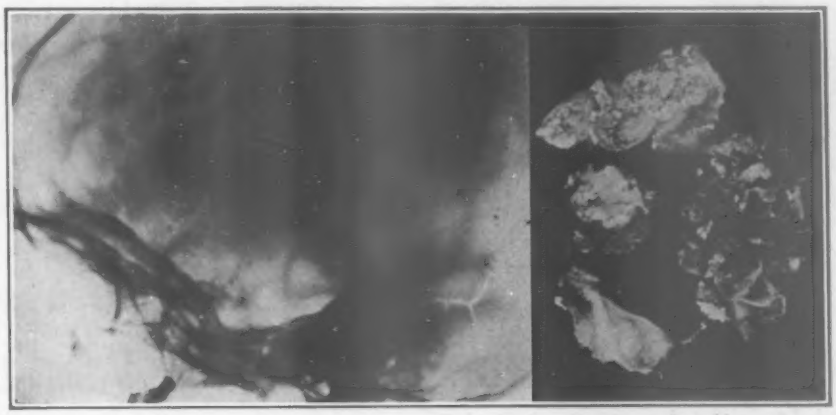

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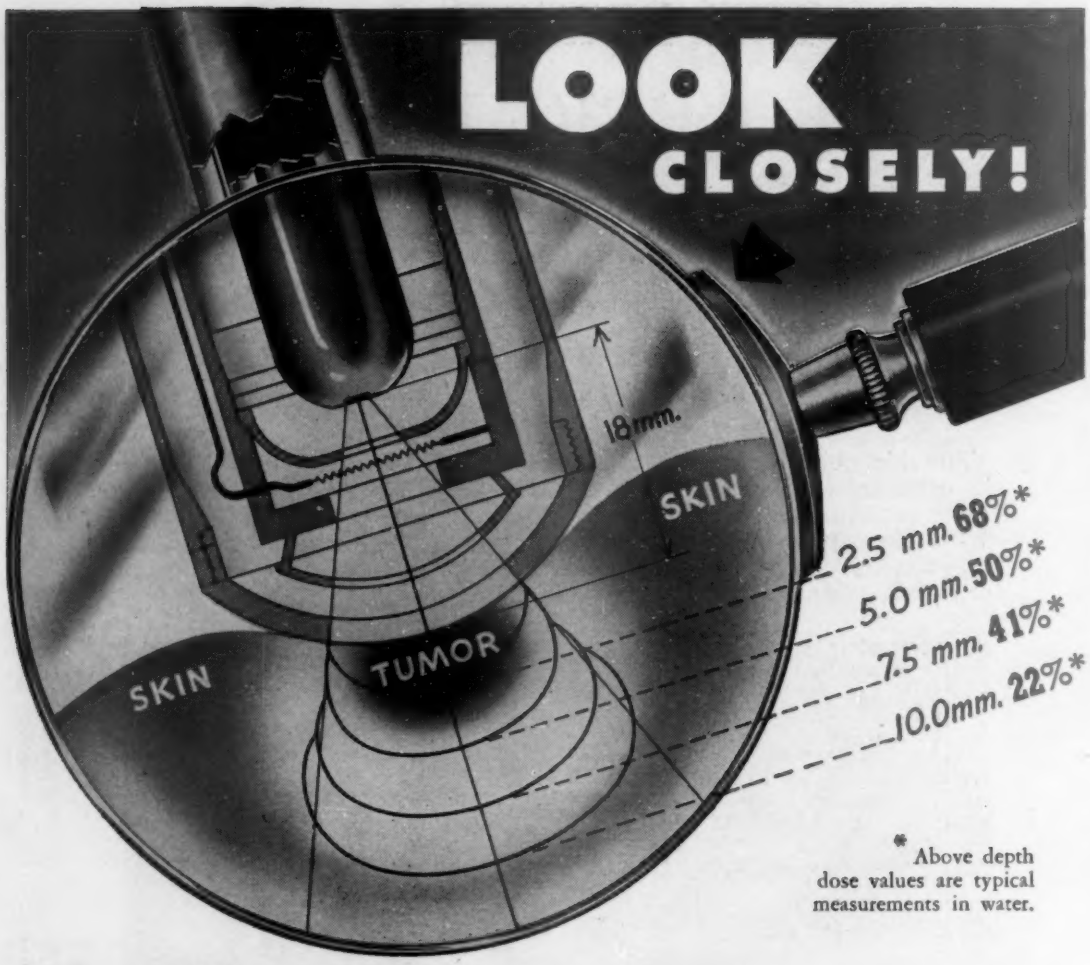

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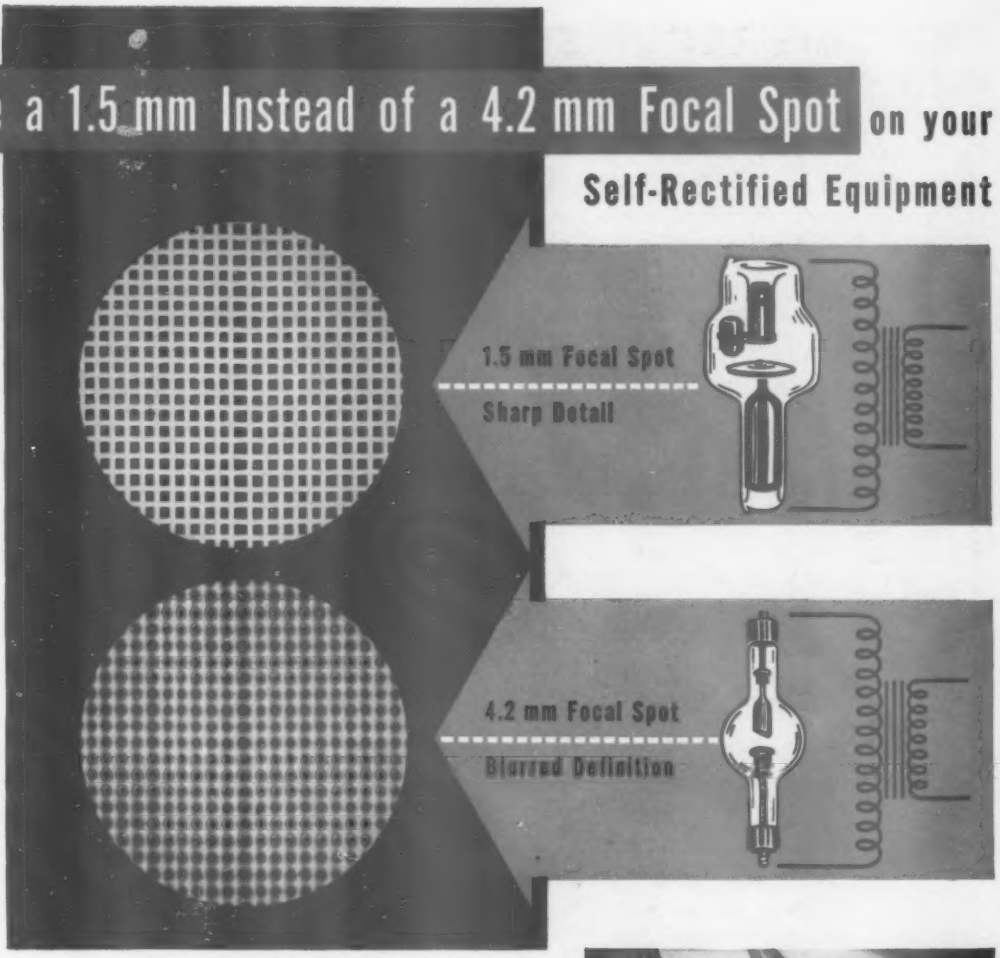

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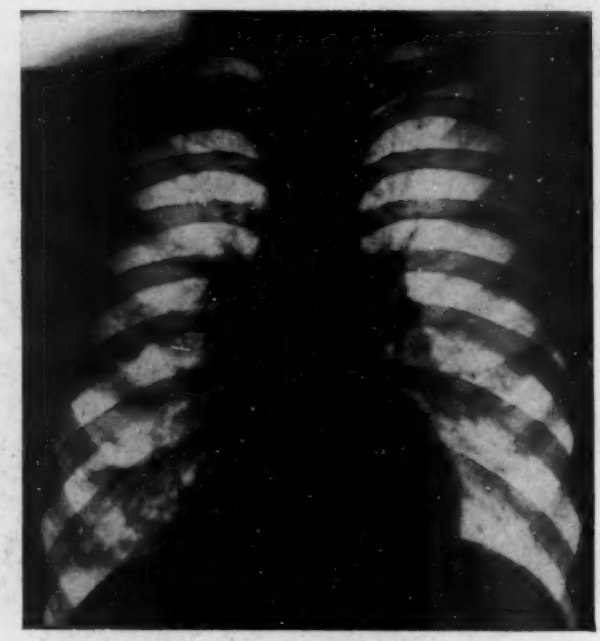

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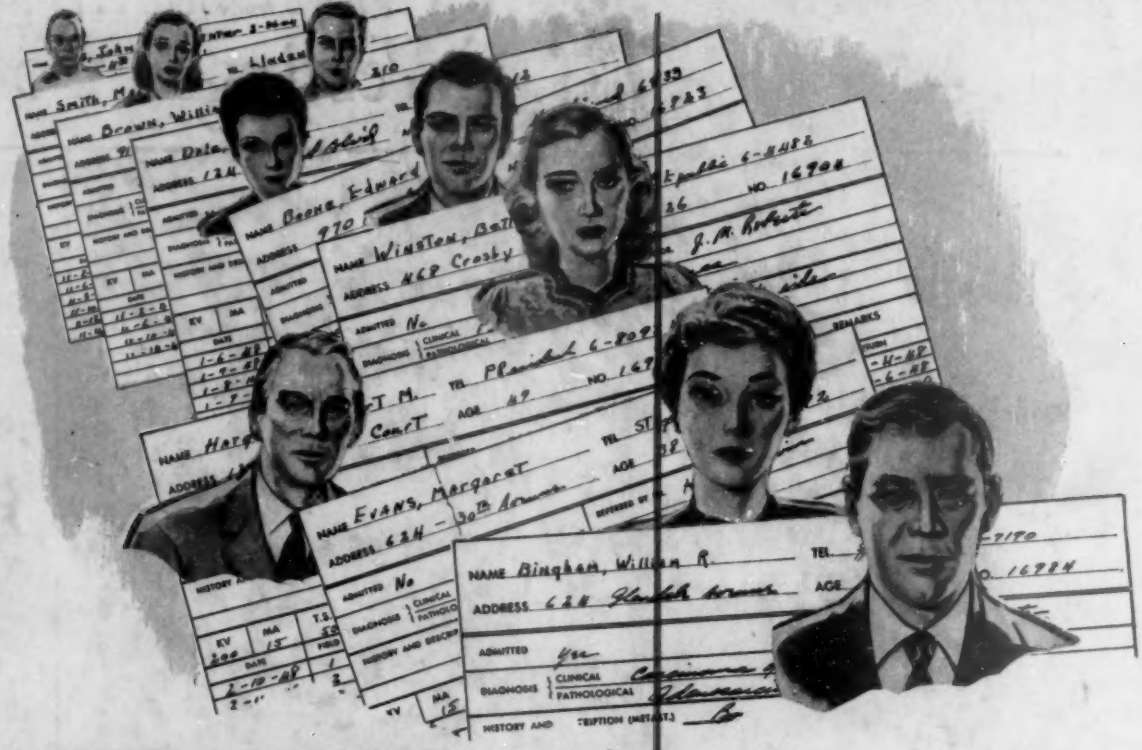
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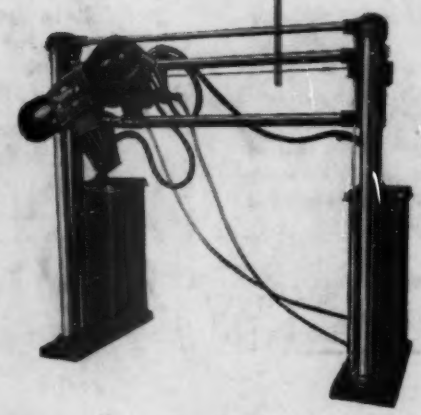

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